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POLYCYSTIC OVARIES IN THE NEWBORN AND EARLY INFANCY AND THEIR RELATION TO THE STRUCTURE OF THE ENDOMETRIUM

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POLYCYSTIC ovaries in the fetus, newborn, and infant are met with sufficient frequency to lose their casuistic interest, although in former times such cases were reported as medical curiosities. As time went on and more cases were reported in the literature, the profession became well acquainted with this condition, but no adequate explanation in regard to its etiology was given until recent times. The first specimen in our series of cases, that of a full-term stillborn fetus, attracted attention by the cystic condition of one of the ovaries. Our interest increased considerably when upon microscopic examination we found the endometrium distinctly hypertrophic and hyperplastic, therefore, we confined our studies not only to the polycystic ovaries, but also to the concomitant changes in the uterine mucosa. In the present work we are concerned with that variety of cystic ovaries in which the cystic structures can be traced to the graafian follicle, and are analogous histologically to that pathologic entity which is designated in the mature woman as "kleineyistische Degeneration" by the Germans and as "l'ovaire à petits kystes" by the French. In reviewing the literature we were amazed to learn of the frequency with which such cases are met, in view of the fact that very little information could be gathered from the textbooks of gynecology upon the subject.

The old pathologists were not unaware of the existence of this condition, and the much quoted Rokitansky (1861) observed cystic follicles in children, in nurslings, and even in fetuses.

DeSinéty (1875) described cystic ovaries in a stillborn at term and in an infant of two days and considered cystic ovaries at puberty a rare occurrence.

Orth's observation (1878) upon this subject concerned the newborn. Von Franqué (1898) found in a three weeks' premature fetus, bilateral cystic structures up to a cherry size, in some of which he could detect the ova.

E. Runge (1906) in a study of 50 cases, comprising fetuses, newborn, and children up to the age of nine years, observed cystic follicles which occurred with greater frequency in infancy and childhood than in intrauterine life.

Benthin (1910) concurred with Runge in his opinion that polycystic ovaries are seen frequently in the newborn and in children.

Delestre (1911) considered cystic follicles in the newborn a very frequent phenomenon and classified these formations as pseudocysts in contradistinction to the cystomas proper of the adult.

Hartmann (1926) studying the process of the ripening of the graafian follicles in the newborn and in children observed quite frequently cystic structures of various dimensions, which in some cases occupied the greater part of the ovary, and which he interpreted as remnants of the graafian follicle.

Newmann (1926) described a full-term stillborn, the right ovary of which contained seven cystic follicles.

Harris (1930) published an article, dealing with polycystic ovaries in an infant two months old. The author made an attempt to explain this occurrence by suggesting the transmission of the mother's pituitary hormone through the placenta.

Newmann (1931), in a series of ten premature and 46 full-term newborns, found in 6 cases large cysts which he likened to the "kleineystische Degeneration" of the adult type, and in 24 cases cystic follicles were seen with the naked eye.

As already stated, in the present study we are concerned with that variety of cystic formations, the origin of which could be distinctly traced to the graafian follicle.

Before we proceed we should like to bring up the question of the presence of graafian follicles in the newborn and in infants, since this has been a matter of much discussion and controversy even up to comparatively recent times. It was commonly believed for quite some time that follicle ripening begins at puberty, in spite of the fact that very early in the history of this question sporadic observations were made to the contrary.

Valisnerus (1739) is quoted by Nagel (1888) and others as possibly the first to observe graafian follicles in young infants and even in embryos.

Grohe (1863) and Raciborsky (1868) both observed graafian follicles in the ripening stage, the former in young children, the latter in a seven-month-old fetus.

Somewhat later Slavjanski (1870 and 1874), who studied the subject extensively, found with regularity growing and ripe graafian follicles from the age of seven days up to puberty; these structures, he thought, in no way differed from those of a mature woman.

DeSinéty (1875), like Slavjanski, was of the opinion that ripening follicles in the newborn and in fetuses are rather the rule than the exception.

The list of observers who found ripening graafian follicles at birth and in childhood could be augmented by mentioning Nagel (1888), Bayer (1902), Runge (1906), Benthin (1910), Delestre (1911), Hartmann (1926), etc. These authors firmly established the fact that some degree of ripening is present at birth or soon thereafter, and that the primordial follicles do not lie dormant until puberty as it was formerly believed.

Assuming from the foregoing that the graafian follicles, whether ripe or ripening, are normal anatomical constituents of the fetal and newborn ovary, we do not mean to imply that every cystic cavity arises from the graafian follicle. Cystic formations of the ovary might have a quite different origin. Olshausen (1877) believed that cystic formations of the ovary may arise from the remnants of the wolffian body (quoted from Lynch and Maxwell, 1922). Babo and von Franqué suggested that some of the ovarian cysts may originate from remnants of the primitive nephros (quoted from Lynch and Maxwell). It is a known fact that the surface epithelium invaginating into the ovarian stroma may form a cyst (Gardner, 1928).

In our material the histologic picture of the structures in question was sufficiently characteristic to enable us to diagnose their source with certainty. The proof *par excellence*, of course, is the presence of the ovum, as no other vesicular structure, than a graafian follicle, possesses it. But while the presence of the egg is an indisputable proof of a follicle, its absence does not speak for the contrary. The cystically degenerated follicle, being an altered structure, frequently loses its egg far in advance of the marked changes in the granulosa layer, and while the latter may yet retain its identity, the ovum may have disappeared or be so degenerated as not to be recognizable at all. We considered a cyst to be derived from a graafian follicle, if the granulosa layer could be detected, or if, perchance, the ovum could be found. Even when the typical granulosa layer was missing as a whole, a few isolated cells, often found upon careful search, enabled us to arrive at a correct diagnosis. Often the presence of other cysts with more typically preserved histologic characteristics in the same specimen was helpful in a difficult situation.

MATERIAL AND TECHNIC

Our material consisted of 36 specimens. The ages varied from the seventh month of fetal life up to the seventh month of extrauterine existence. Seven were stillborn, 2 of which were eight months prematures, 12 lived from two and a half hours to four days, 13 were from three weeks to seven months old, and 4 other premature fetuses of seven and a half and eight months. As for the last group we were unable to ascertain from the histories available whether some of the fetuses were born dead or alive. Summing up we may say that there were 23 newborns, at term or premature, and 13 infants from three weeks up to seven months. In the newborn group there were eleven prematures.

Twenty-nine pairs of ovaries were inspected and sectioned, and in the other 7 cases a single ovary was sectioned, but both were inspected for the presence of cysts. In 15 cases cystic structures were found, five times unilaterally, ten times bilaterally. Out of the unilateral group, one, upon histologic study, proved to be not a follicle cyst but a paraovarian. Thus there were 14 follicle cysts among 36 cases, an incidence of 39 per cent in the whole group. The smallest cyst measured 1 mm. (in one case only), the largest measured 1.5 cm., the majority averaging from 5 to 6 mm. All measurements, for reasons not depending upon us, were taken after fixation, a fact which distorts the actual figures. The causes of death were manifold: intracranial hemorrhages, atelectasis of the lungs, hydrocephalus, pneumonia, prematurity, congenital heart anomalies and duodenal obstruction. These were among the anatomical diagnoses of the fetuses and the newborn. Bronchopneumonia, operative procedures, infectious diarrhea, etc., were given as the causes of death in the older infants. Accessory spleen in one case and congenital shortening of one limb in another were among the interesting incidental findings.

The infants were brought into the world either by normal delivery or by operative procedure, including Porro's cesarean section. In 11 cases the cysts were found in infants over three weeks of age, in 3 cases they were in the newborn, twice in a full-term stillborn, once in a full-term newborn, who lived four days. The paraovarian cyst belonged to a seven months' premature fetus that lived two and a half hours. The uteri were sectioned approximately on the same level, namely, on the level between the upper and middle thirds of the corpus uteri. We deliberately avoided the lower portion of what we thought was the uterine body, because the cervix at this age is not clearly delineated and plicae palmatae could be seen at various levels. The smallest uterus measured from fundus to cervix 10 by 5 by 3 mm., the largest measured 43 by 16 by 5 mm. in a full-term stillborn, thus exceeding by far the size of each of the two seven-month-old infants in our series, in which the uteri measured 15 by 10 by 4 mm. and 29 by 18 by 5 mm., respectively.

The ovaries of the same specimen were found sometimes unequal in size, not only when one was cystic, but also when both appeared normal. The largest ovary was found in a seven-week-old baby, measuring 29 by 4 by 1 mm., and which contained a small cyst. The two oldest infants in our series, each of seven months, had ovaries of the following dimensions: 15 by 6 by 2 mm., 13 by 5.5 by 2 mm., and 22 by 10 by 5 mm., 22 by 6 by 5 mm., respectively. Longitudinal sections of both ovaries were made in such a manner as to include the region of the hilus. Circular sections of the uteri were made involving the whole thickness of the organ. Hemalum and eosin were used as a routine stain. In a number of cases we availed ourselves of Van Gieson's method, and in a few instances only, for better nuclear study, we utilized the phosphotungstic acid stain.

Histologic Findings.—We studied the ovaries minutely stressing particularly the fine structures of the cystic cavities. The cystic formations differed somewhat in detail, although in general their architecture was similar to one another. The granulosa layer was almost always found in the cysts and even when not seen in large amounts, we found a few isolated cells in their cavity, and only very few cysts were devoid of this structure altogether. Sometimes we observed the granulosa layer considerably thinned out and reduced in some areas to one row of cells, which lined the cystic wall, but more often we saw the epithelial structure detached and floating freely within the follicular cavity. The cells had a tendency to group themselves into bizarre figures, forming either linear or solid strands. For the most part, the individual cells possessed a small body of polyhedral shape, the borderlines of which were not distinct. The nuclei were of moderate size,

occupying the larger part of the cell, of oval or round shape, and occasionally semilunar nuclei were noted.

The chromatic material was intensely stained, appearing as dark, coarse, distinct granules; the nuclear membrane was well outlined, and a considerable number of mitotic figures were observed among the hyperchromatic nuclei. Alongside the pyknotic granulosa cells, there were others, which showed considerable less affinity for the basic stains. These pale cells were sometimes indistinguishable from the light pink material which filled the cavity so that if not for the well-outlined nuclear membrane, such structures could not have been recognized as cells. In a small number of cells we saw vacuoles within the substances of the protoplasm.

The follicular fluid within the cystic cavities was either finely granular, or reticular, or amorphous in appearance. Its staining properties varied from pale pink to an intensely reddish pink, and variously sized vacuoles were not seldom seen. The walls of the cysts varied greatly in thickness, and the larger the cysts, the thinner the wall appeared to be. The theca interna consisted of spindle-shaped cells, the nuclei of which were considerably lighter than those of the granulosa layer.

Nuclear figures were noted occasionally. In some cases the theca interna layer formed a rather thick covering, and the cells appeared large with lightly stained nuclei and very light, almost transparent, protoplasm, giving to this structure a resemblance to lutein cells. In a very few instances the cells of the theca interna assumed a radial direction, in contrast to the theca externa, which preserved at all times its circular course.

The outer layer, the theca externa, consisted of connective tissue stroma and connective tissue cells, which formed a narrow shell around the follicle, not clearly delineated from the rest of the ovarian stroma. The nuclei of this layer were more hyperchromatic than in the theca interna, but less than in the granulosa cells. In a small group of cysts, the wall in some places formed protrusions within the cavity so that the contour of the inner surface became wavy. In no large cysts did we detect the ovum and only two of the smaller ones revealed this structure.

In the noncystic ovaries and in the noncystic parts of the cystic ones, we saw all the usual constituents ascribed to them. Many primordial follicles with light, large protoplasm of the ovum and well-outlined nuclei were the rule. In a considerable number of cases the nuclei were faded, or had almost disappeared. The protoplasm of the egg in a large number of cases appeared foamy and its limits were not always sharply outlined.

The granulosa layer consisted of one row of flattened cells which surrounded the ovum. Not seldom two nuclei in one ovum were noted. Various degrees of development of the graafian follicles were found and only in 7 cases were they missing altogether. Since the only indisputable sign of a fully ripe graafian follicle, namely, the maturation of the ovum, was not sought, we do not know whether we saw fully developed follicles in our series. But often structures of various dimensions were observed, possessing theca interna and externa, the ova of which with their zona pellucida and corona radiata, were located on a cumulus oophorus, and the granulosa layer of which was many layered and abundant. Differentiation of the ovum into protoplasm and deutoplasm was not observed.

Atretic follicles, some of which had a distinctly thickened membrana propria, were met with great frequency and quite often corpora candidantia were found. In some cases polyovular follicles and in some follicles polynuclear ova were seen. Several of the ovaries showed an increased vascularity.

Summarizing, the histologic findings in the ovaries are as follows:

1. Cystic follicles were found in 39 per cent of the cases in the whole group.
2. The granulosa was found pycnotic most of the time; karyolysis and karyorrhexis were also seen.
3. Partial autolysis of both nucleus and protoplasm and also vacuoles were observed.
4. The granulosa layer was most often detached from the cystic wall and free within its cavity.
5. The theca interna in a few cases only acquired the characteristics of theca lutein cells.
6. No ovum was found in the large cysts.
7. Primordial follicles were seen in all of the specimens.
8. Growing and maturing follicles were observed in all but 7 cases.
9. Polyovular follicles and polynuclear ova were noted.
10. Vascularity of the ovaries was a frequent occurrence.

The chief object of this work was to correlate the histologic picture of the endometrium with that of the polycystic ovaries in the newborn and infant, and naturally, we were looking for signs of hypertrophy and hyperplasia in the glandular constituents of the uterine mucosa.

The older clinicians observed from anatomopathologic material that the female generative tract is proportionately larger in late fetal life than in infancy and childhood.

Lyubetski (1900) is quoted by Scammon (1926) as being the first to describe the retrogressive changes occurring in the first weeks of extrauterine life.

Bayer (1902) stated that a considerable growth of the uterus occurs in the last two months of fetal life and that a marked decrease in size is seen after birth, and he spoke of it in terms of postfetal involution.

Halban (1904) not only observed this fact, but attempted to give an explanation to this phenomenon which in part has withstood the test of time (his views will be elucidated later).

Scammon (1926) believed that between birth and the age of three weeks of extrauterine life, the uterus, on the average, loses about 11 mm.

Newmann (1931) cited two cases in order to add additional proof to the contentions of the above-mentioned authors.

While Halban described changes in the fetal endometrium, ranging from hyperemia to premenstrual hypertrophy and hyperplasia, there were others who thought that the fetal uterus, even in later intrauterine life, is in a rudimentary stage of development and that the glandular structures of the corpus are lacking.

Such was the state of knowledge when Kundrat (1873) expressed a view that the uterine glands first make their appearance at the age of one year (quoted from Wyder 1878).

Engelmann (1875) stated that glands in the endometrium of children began to manifest themselves between the ages of three to four years.

Wyder (1878) observed glands in the newborn's uteri, but with no regularity.

Möricke (1881) came closer to the truth, believing that every newborn possesses glands in its uterine mucosa.

Meyer (1898), too, observed glands in the newborn not infrequently.

As late as 1909 Bailey and Miller in their textbook of Embryology stated that uterine glands develop after birth between the ages of one and five years and that their development is not completed until the age of puberty.

Schroeder, in recent times (1930), believed that glands were present at birth and in childhood but that there are individual variations in their number.

In our own material we saw glands in all but four cases. Of the latter one specimen belonged to a two-month-old infant, two others to two premature fetuses of seven and one half and eight months respectively, and the fourth was obtained from a six-hour-old full-term baby. The number of glands varied between one and 53 in all fields of one cross-section.

Out of all the uteri only 5 showed distinct and pronounced signs of hypertrophy and hyperplasia of the glandular elements. These 5 were obtained from 3 full-term stillborns, from one five-hour-old infant born at term, and from one seven and one-half month premature fetus. The glands of this group were numerous, varying in number from 13 to 53, large, tortuous, lined with high cylindrical epithelium, which appeared stratified in some places. Tubular, but widened in some areas, tortuous and corkscrew in others, and filled with mucoid substances, these glands gave a striking appearance of proliferative and secretory activity. In many regions the individual epithelial cells were unusually high and their staining properties were very feeble, becoming almost transparent at their base.

The inner border of the cylindrical epithelium in a few glands lost its smoothness and evenness, becoming distinctly frayed. The nuclei were oval shaped and situated in the middle portion of the pale cell. In short, we saw a picture very similar to the proliferating and secretory phases of the menstrual cycle in the adult woman. The surface epithelium bore a close resemblance to the glandular. The uterine cavity in all these five cases was filled with a lightly stained mucus-like substance. The rest of the cases presented rather varied pictures. In them the surface epithelium was either cuboidal or low cylindrical, and often in some areas it was missing altogether. The cavities contained either a mucus-like substance, or desquamated epithelium, or a structure much resembling endometrial stroma. Invaginations of the surface epithelium into the stroma were sometimes deep, sometimes shallow and often numerous. The number of glands were very few. In some cases no more than one was encountered, while in other cases, as many as eighteen were seen. But whenever the glands were narrow, small and lined with one row of cylindrical epithelium, which bore no marked signs of activity, they were not considered of the hyperplastic group. Even though occasionally a slight tortuosity of one or two glands was seen in the nonhyperplastic group, and even though signs of secretory activity were occasionally observed in the same group, nevertheless only pronounced changes in the glands, involving their number, shape, size, and epithelial structure were relied upon in the diagnosis of hypertrophy and hyperplasia of the endometrium.

The endometrial stroma was found loose or dense, consisting of spindle and fusiform cells. Except for one specimen in which there were distinct hemorrhagic areas and an extreme development of blood vessels throughout the whole organ no peculiarities, worth mentioning, were observed.

DISCUSSION

Since sufficient evidence began to accumulate in the periodic literature, concerning the relatively large size of the newborn's uterus, many attempts were made to explain this occurrence.

Halban (1904) on the basis of clinical material mainly offered an explanation which has found partial corroboration in the experimental work done since. He believed that the hypertrophic condition of the uterus is due to active principles present in the mother and derived from the placenta. Numerous experiments have proved that placental and ovarian extracts have a profound influence upon the growth of the uterus. The number of investigators in this field of endocrinology is too large to enumerate, but we shall mention just a few works of more recent times.

Aschner (1913), working with ovarian and placental extracts administered subcutaneously, found hyperemia of the uterus and excessive growth of the graafian follicles in the test animal.

Herrmann (1915) by injecting corpus luteum and placental extracts into immature rabbits observed a powerful influence upon the whole genital tract (vulva, vagina, uterus, tubes and ovaries). Similar experiments upon rabbits with the production of hyperplasia and hypertrophy of the uterus were made by Frank and Rosenbloom (1915) and by Frank (1917).

It was a well-known clinical fact that castration of females produced pronounced changes in the accessory genital organs (Lipschütz, 1924).

Experimental gonadectomy in the immature female mammals and other species enable the research worker to control the growth of the uterus at will (Lipschütz, 1924). Ovarian transplantation, studied extensively by Lipschütz and Pettinari, was another factor in demonstrating the profound influence of the ovaries upon the well-being and growth of the uterus.

It was further observed that ovarian extracts could produce a characteristic syndrome in the immature or mature animal, namely, they could cause or expedite estrus (literature given by Frank, 1929).

It was also learned that no matter what part of the ovary the extracts came whether from whole ovary, follicle wall, follicle fluid, residual tissue, or corpus luteum, the results upon the animal were the same, namely, estrus (Frank, 1929, Zondek, 1931, and others).

For the sake of completeness we must add that the corpus luteum is not regarded by all as containing the estrus-producing hormone (Parkes, 1929). Furthermore, it became known that estrus could be produced when placental extracts or amniotic fluid were used (Frank, 1929 and Zondek, 1931).

The active substance contained in these extracts was variously called "female sex hormone," "estrin," "folliculin," "menformon," "feminin," "thelykinin," etc. (Parkes).

Uteri of various animals, stimulated by the female sex hormone, were found enlarged, their mucosa showed marked changes, such as an increase in the number and size of the glands, also the shape of the glandular elements was altered, and products of their secretory activity could be seen.

From another series of very interesting experiments it was evident that a transplanted ovary either flourishes or perishes, depending, besides other factors, upon the age of the host.

Foa (1900) demonstrated that by grafting embryonic ovaries upon a mature animal, a great rapidity of maturation of these gonads was produced (quoted from Pettinari, 1928).

Lipschütz (1925) made similar observations with the conclusions that the age of the host influences the condition of the ovarian graft.

It was also observed that the female sex hormone, stimulating the accessory generative organs, does not, however, affect the ovaries, neither functionally, nor histologically (Aschheim and Zondek, 1928, and others).

From such and similar experiments the supposition was made that the ovary itself needs an extraneous agent for its activation. Such influences were sought in other glands of internal secretion and among them in the hypophysis. Again, an important clue came from clinical facts.

Cushing (1912) stated that there is a close relationship between the function of the pituitary body and that of the ovary.

Aschner (1912) by total or partial extirpation of the pituitary gland produced a retardation of the growth of the ovaries in the immature dog. On the other hand it was well known that bilateral gonadectomy produces alterations in the hypophysis of the castrated animal (Pettinari, 1928).

Evans (1924), using saline extracts of the anterior lobe of the pituitary gland, observed corpora lutea formation in the ovaries of the tested animal.

Further research brought out the important fact that the transplantation of the anterior lobe into immature female mice caused precocious maturity of the animal and was accompanied by significant changes in the ovaries, such as ripening of the follicles, hyperemia and even the maturation of the ovum (Zondek, 1926, and Zondek and Aschheim, 1927).

Smith (1926) came to similar conclusions working with homoplastic transplants upon immature rats. About the same time another phenomenon was observed, namely, that not only follicles ripened, after anterior lobe transplantation, but in some cases in mature animals they underwent a cystic transformation (Smith, 1926, and Engle and Smith, 1929).

Summarizing the above we may say that while the accessory reproductive organs are dependent upon the function of the ovaries, the latter in their turn, are influenced by the anterior lobe of the hypophysis, which is defined by Zondek as the "motor of the sexual function."

In another series of experiments the female sex hormone (Frank, 1929) and the anterior pituitary hormone were found in large quantities in pregnant women, the urine and blood of whom are virtually loaded with these substances (Aschheim and Zondek, 1927 and 1928).

On the other hand the same two hormones were found with more or less regularity in the newborn, irrespective of sex, in the first few days of life. Important contributions in this field, confirming the above-mentioned fact, were made by Philipp (1929), Brühl (1929), Newmann (1931), and Winter (1932).

Zondek (1931), too, found these hormones in the newborn with frequency, but, however, with no regularity.

With the above information at hand we shall endeavor to analyze our own material to see whether anatomopathologic facts could clear up some obscure questions. As it was said before, we found five uteri with very marked hypertrophic and hyperplastic changes in the uterine mucosa, the same type of changes which could be produced experimentally by the female sex hormone. It is logical to assume that these

structural changes in the endometrium were produced by the female sex hormone, almost constantly found in the newborn in the first few days of life. And since the hyperplastic changes in all these five speci-

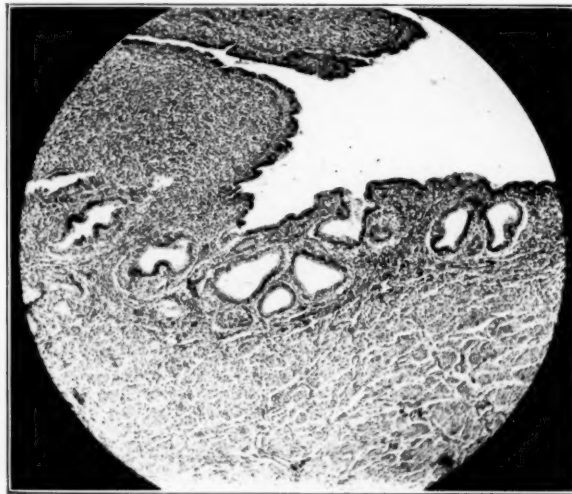


Fig. 1.—Uterus. Full-term stillborn. The endometrium is hyperplastic and hypertrophic, the glands are somewhat tortuous, dilated and contain mucous debris in their lumina.

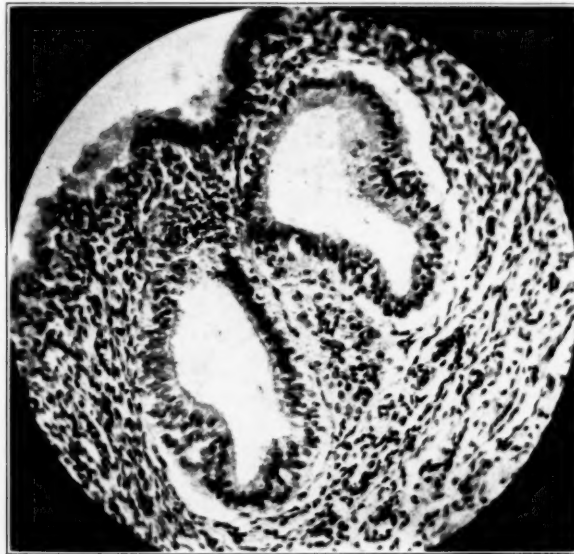


Fig. 2.—The same specimen under higher magnification. The glands reveal their high cylindrical epithelium, which is stratified in some areas. The transparency of the cells at their base, the frayed contour of the inner surface and the mucoid debris are clearly seen.

mens were found at birth, we may say that this condition was congenital in at least our series of cases.

Almost all newborn, it has been proved, have female sex hormone

in their urine and blood, but only a few of them, as our material tends to show, have hypertrophic and hyperplastic endometrium. Possibly there are quantitative variations of estrin in the newborn which could explain satisfactorily this seeming discrepancy. Several uteri, not classified by us as hyperplastic, showed in some areas signs of either secretory activity, or some tortuosity of one or more glands, or a slight proliferation of the epithelium. These signs were too mild to classify these uteri as hyperplastic for we were looking for marked changes in the mucosa. Nevertheless, there is a possibility that these mild signs of secretory activity and proliferation are due to the presence of estrin, the amount of which is not sufficient for more pronounced changes. In other words, these individual variations in the size and number of glands which were described as normal for the newborn (Schroeder,

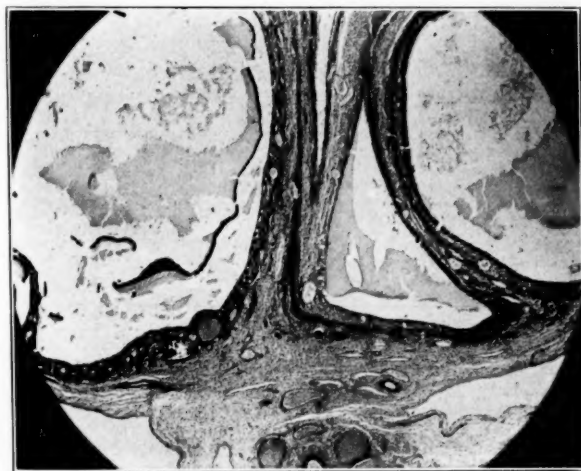


Fig. 3.—The polycystic ovary of the same specimen. There are seen large cavities with hyperchromatic granulosa cells, which are either attached to the cystic wall or free within the cystic lumina. The theca interna is quite vascular. Follicle fluid fills the cavities.

1930) may be just a response to a mild stimulation by the female sex hormone. We do not know what causes this supposed variation in the quantity of estrin, we only assume that the difference may exist.

Allen et al. (1924) experimented with extracts of follicle contents and induced a condition of the genital organs in the spayed rats similar to that of the mature animal. In other words, according to these investigators, cystic follicles possess hormonal activity.

We were looking for the source of such hormonal activity in the ovaries of these five cases in which the uteri were hyperplastic. In only two of the five cases of the hyperplastic group did the ovaries possess cystic follicles. One case was that of a full-term stillborn, one ovary of which contained several cysts, the combined diameter of which measured 1 cm. (Figs. 1, 2, 3). The other case, also a full-term newborn, had a single, small cyst not exceeding 1 mm. in diameter which

was situated in the depth of the organ, which strictly speaking, was not a polycystic ovary, since it had one cyst only. In this last case with so few changes in the ovary, the uterine mucosa showed most striking signs of hyperplasia, hypertrophy, and secretory activity, excelling in these features any other specimen in the whole series (Microphotograph P.M.W.) (Fig. 4).

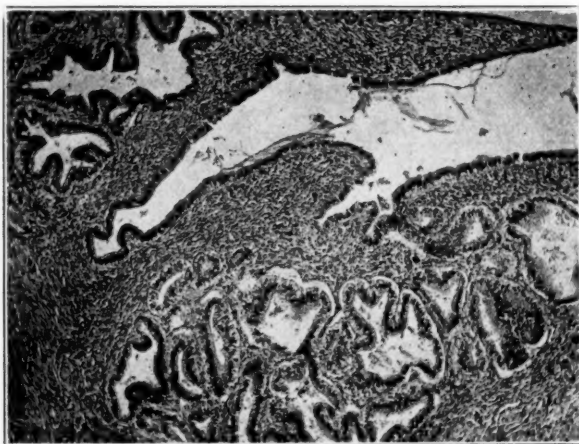


Fig. 4.—Very striking changes in the endometrium of a full-term stillborn. Tortuosity of the glands and their secretory activity are very pronounced (one of its ovaries had a single, very small cyst). $\times 90$.

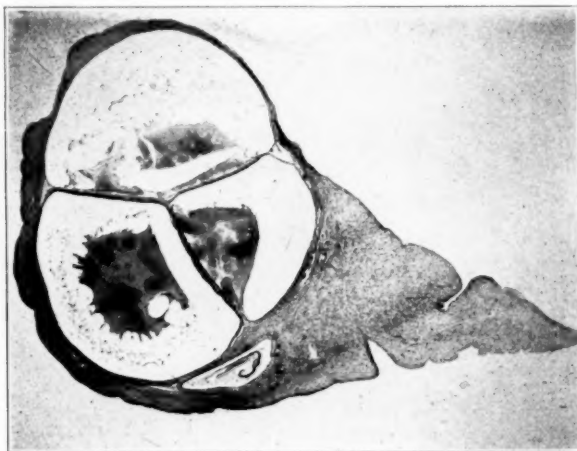


Fig. 5.—One of the bilateral polycystic ovaries from a five-month-old child. The cystic cavities, divided by narrow septa, occupy the major part of the ovary. The uterus of this case is mildly stimulated, but not distinctly hyperplastic. $\times 8$.

Taking into consideration the fact that in the hyperplastic group the majority of cases did not possess polycystic ovaries, and also the fact that the cystic alterations in the ovaries, whenever present, were not commensurate with the degree of endometrial hyperplasia, we may say that the signs of proliferation were not probably due to the cystic changes in the gonads (we shall strengthen this fact somewhat later).

We will conclude the discussion of hyperplastic uteri by stating, first, that this condition in our cases was congenital only, and second, it did not presumably depend upon the cystic degeneration of the ovaries. While it was sufficiently simple to interpret the condition of the uterine mucosa in relation to the cystic ovaries in the newborn, it is still simpler in the infant for none of the infants from three weeks up to seven months showed distinct signs of hyperplasia.



Fig. 6.—Ovary from a seven-month-old infant. One of the bilateral cystic ovaries. Three cysts are present in this ovary. One of them is subdivided into two by a septum. An atretic follicle is visible laterally. Considerable vascularity throughout the whole organ is a prominent feature of this slide. $\times 10$.

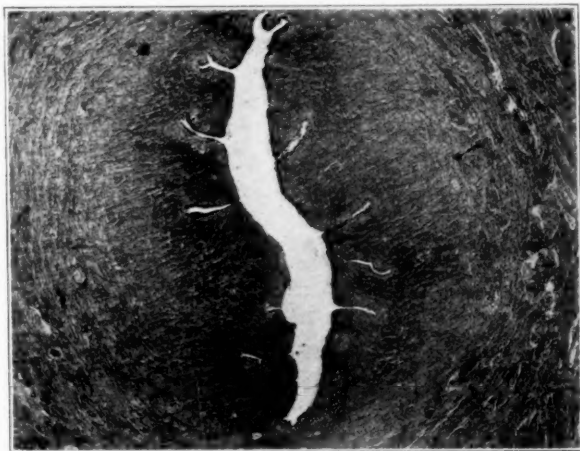


Fig. 7.—Section of uterus of the same case. Endometrium devoid of glands (the single gland present did not enter the field), shallow invaginations. $\times 41$.

In one case only, in that of a five-month-old infant whose ovaries underwent a bilateral cystic degeneration and the cysts of which occupied the major part of the organs (see Fig. 5), did the uterine mucosa show a very mild degree of secretory activity. In this case the glands were neither numerous nor enlarged but in some of them the lumina contained mucoid-like substance and their epithelium was higher than usual. Nevertheless, these endometrial changes were not sufficiently

pronounced to be placed in the hyperplastic group. We may safely say that in the infants the endometrium did not show, as a rule, signs of being stimulated by the female sex hormone which the cystic fluid was expected to contain.

Since the polycystic ovaries in infants of nursling age have not produced in the great majority of cases a stimulation of their corresponding uteri (Figs. 6 and 7), we may now be more certain about the same negative relationship in the newborn group, and may consider the polycystic ovaries, in the two cases already mentioned, of that group as an incidental finding.

How explain the occurrence of polycystic ovaries in the newborn? There are enough facts in the experimental field (we cited them above) to show that the newborn contains the anterior pituitary hormone in his urine and blood. On the other hand, we learned from Engle and Smith that anterior pituitary hormone can produce cystic follicles in the ovaries (in their experiments the cysts were produced in the mature animal). This fact, in conjunction with the above mentioned leads us to the supposition that the cystic follicles in the newborn are produced by the anterior pituitary hormone.

Harris, as already mentioned, suggested that the fetus gets its anterior pituitary hormone from the mother through placental transmission. We do not know whether the newborn derives this hormone while in utero, through or from the placenta, which is also a rich source of this hormone, or in any other manner. All we can say is that we know nothing to contradict the possibility of the fetus receiving this hormone from either of the above-mentioned sources.

Much more puzzling to us was the occurrence of polycystic ovaries in the infants. Tabulating our material according to their ages, we find that the majority of polycystic ovaries occurred not in the newborn but in infants, as Table I shows.

TABLE I

AGE	NO. OF CASES	TERM (OR NOT)	HYPERPLASIA OF THE MUCOSA
Stillborn	1	Yes	Yes
Stillborn	1	Yes	Yes
4 days	1	Yes	No
3 weeks	1	Yes	No
4 weeks	2	Yes	No
7 weeks	2	Yes	No
2 months	1	Yes	No
3 months	1	Yes	No
3 ½ months	1	Unknown	No
5 months	1	Unknown	No
6 months	1	Yes	No
7 months	1	Unknown	No

We can clearly see that only three belonged to the newborn group and eleven to the infants, an incidence of 13 per cent and 85 per cent respectively (we had 23 newborns and 13 infants).

Classifying the newborn at term separately from the prematures, we still have three cases of polycystic ovaries in twelve full-term newborns, or an incidence of 25 per cent in this last group. Infants of three weeks or older we did not classify as newborn. We chose three weeks as the borderline between the newborn and the infants because at this period, according to the old and new literature, postfetal involution of the genital organs is completed. We do not know to what extent our material is typical of such findings, but it is interesting that in our series of cases, such a striking predominance of polycystic ovaries in infants, in contrast to the newborn, was found.

The material of Runge and Benthin seems to sustain our figures. The former saw polycystic ovaries in fetuses in 10 per cent of the cases, in the newborn at term in 18 per cent, and in the second year of life in 85 per cent. The latter observed cystic follicles at the age of nine months, ten months, one year, two years, etc., up to nine years of age. Assuming that the cystic structures are formed in late intrauterine life, and that they persist in extrauterine life, then we must admit a great longevity of these cysts for they were found throughout the whole childhood (Runge and Benthin). But the above assumption would seem to be refuted by the experience of Engle and Smith (1929), in whose experiments the cysts were short-lived and became obliterated within eight days after the last transplantation of the hypophysis. If all the cystic follicles in infants were of congenital origin, we should expect, approximately, the same incidence of occurrence in the newborn as in the infants and older children. Allowances, of course, should be made for variations in statistical material, and also possibly for the fact that we were dealing with a comparatively large number of prematures, none of whom, however, was younger than the seventh solar month. The difference in our figures of 13 per cent for the whole newborn group (or 25 per cent for the full-term group), and 85 per cent for the infants, and also Runge's 18 per cent for the newborn, and 85 per cent for the second year of life, is too great to attribute to normal variations.

A few observations were made to the effect that the hypophyses of swine fetuses and newborn, implanted into immature mice, produced positive effects upon the latter's ovaries, proving that hormonal activity of this gland is present at a very early age in the tested species (Philipp, 1929).

The same author stated that anterior pituitary hormone was found occasionally in growing children (one year, two years, eight years). Do not these observations add some strength to our supposition that not all cystic ovaries in infants are of congenital origin? On the basis of our material we are inclined to suggest the possibility of polycystic ovaries in the infants, in some instances, arising in extrauterine life.

CONCLUSIONS

1. In a study of 36 cases, comprising fetuses, newborn, and infants, five of the newborns showed hyperplastic endometrium, an incidence of 14 per cent for the whole group, and 22 per cent for the newborn group, prematures and full term included.

2. In no instance were there found distinct hypertrophic and hyperplastic uterine mucosae in the infants (one case of very mild stimulation was noted).

3. Coexistence of polycystic ovaries and hyperplastic endometrium was observed twice in the newborn group only.

4. Polycystic ovaries were found predominantly in infants, namely in 85 per cent, while in the newborn the incidence of this condition was 13 per cent, or in the newborn at term, 25 per cent.

5. Polycystic ovaries in infants of three weeks and older were not associated as a rule with hyperplastic and hypertrophic endometrium.

6. There seems to be no causative relationship between cystic follicles of the ovaries and the structure of the endometrium in the newborn and in infants.

7. In view of the greater predominance of polycystic ovaries in infants in comparison to the newborn, a suggestion is made that cystic degeneration of the follicles may be extrauterine in origin and may possibly depend upon the infant's own pituitary activity.

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TUBERCULOSIS OF THE UTERUS AND FALLOPIAN TUBES WITH A REPORT OF TWO CASES TREATED WITH X-RAYS

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ALTHOUGH not a rare condition, but few gynecologists encounter a sufficient number of cases of tuberculosis of the female internal genital organs during the course of a year to be able to evaluate the efficacy and results of the various methods of treatment now available. The frequent impossibility of making a diagnosis of the true nature of the lesion at operation as well as the widespread use of conservative measures and diathermy in acute and subacute salpingitides in which an accurate diagnosis of the etiology is lacking, have further prevented the accumulation of data on the natural history of the disease. For these reasons, a rather extensive analysis of the results obtained by the various methods of treatment, as controlled by adequate follow-up statistics and reported in the literature was made. The findings were considered to be of sufficient interest and importance to warrant this report.

The outstanding result of these studies has been to show how unsatisfactory are the results of treatment of tuberculous adnexitis and metritis by our present methods. While conceding that some cases must remain undiagnosed and are cured without the patient or her physician being aware of its presence, statistics from various sources tend to show that genital tuberculosis in its clinical stages has a grave prognosis when untreated or subjected to medical measures alone. In a fairly large autopsy experience on tuberculous women, we have failed to find a case of healed pelvic tuberculosis and no reports of such cases have been found in the literature. On the other hand, the primary mortality of the various series of operated cases averages about 7 per cent, with a subsequent or secondary mortality, as shown by follow-up statistics, of 21.7 per cent. There is no doubt that the mortality of the occasional operator and in less well-selected cases is much higher.

While it is true that genital tuberculosis, like tuberculosis elsewhere in the body, shows an innate tendency to heal, experience has amply demonstrated the falsity of the contentions of Krönig, Veit, Hegar, and Hofmeier that it heals spontaneously, that it never encroaches on other

organs or gives rise to fistulas, and that it never causes death directly or indirectly. More accurate methods of diagnosis and closer check-ups on the subsequent course of the disease have shown that intervention of some sort is necessary to effect a cure.

At the present time the advocates of the "hands-off" policy are in a minority and the tendency of the interventionists is to adopt an eclectic attitude in which some attempt is made to individualize the cases and employ surgical measures based upon the apparent extent of the disease as well as the age and general condition of the patient. With the exception of certain French gynecologists, the sharp distinction between the proponents of conservative surgery in all cases and those who recommend more radical procedures has largely disappeared. At the present time the nonoperative or conservative surgical treatment group is represented by Labhardt, Weibel, Bumm, Döderlein, Schauta, Vanverts and his pupil Eloy, Pestalozza and a few others; the sponsors of the radical measures, which in most cases is understood to comprise supracervical hysterectomy and bilateral salpingectomy with conservation of the ovaries when possible, include von Franqué, Fehling, Douay, Faure, Albertin, Daniel, and Peterson.

The advocates of conservative surgery in tuberculosis of the adnexa are following excellent gynecologic principles in wishing to remove only diseased tissue and to conserve, so far as possible, uninvolved structures. The principal objection to the doctrine as applied to tuberculosis of the pelvic organs is that *it is absolutely impossible to determine the extent of the disease macroscopically*. Various statistics tend to show that tuberculous salpingitis is bilateral in well over 90 per cent of cases. The true incidence of uterine tuberculosis in cases of tuberculous salpingitis is impossible to estimate, as the organ has not been routinely removed in most series, but there is evidence that the figure is well over 50 per cent. Faced with such a possibility, it is a bold operator indeed who would be satisfied with a unilateral salpingectomy or conservation of the uterus when both tubes are extensively diseased unless very good reasons existed why a chance of incomplete removal of the focus and recurrence should be taken.

The work of Sir Spencer Wells in 1862 showed the efficacy of simple laparotomy in the ascitic type of tuberculous peritonitis and his observations have been repeatedly reaffirmed since that time. In the 12 cases reported by Peterson in which exploratory laparotomy and biopsy only were done in the presence of tuberculous peritonitis, 50 per cent were living and well from one to eighteen years later and Vautrin has recorded 25 successes in 34 such operations. In the 6 cases of Villard in which a simple laparotomy was done and which were followed for a long period of time, there were four cures and two durable improvements. Ashby has obtained 65 per cent permanent recoveries in the ascitic type of peritonitis by laparotomy alone. In the serosal type of tuberculous

salpingitis, which is usually found associated with ascitic tuberculous peritonitis, the tubercles are limited to the peritoneal surface of the tubes and uterus and the lesions are entirely analogous to those found on the other abdominal organs. In such cases there is no indication for removal of the organs and numerous instances have been recorded by Leriche, Villard, and others in which reoperation one to twelve years later has shown complete regression of the tuberculosis. The peritoneal granulations form hard white spots which in many cases are entirely absorbed, with a return to normal of the pliancy and glistening appearance of the peritoneum. The removal of the ascitic fluid, combined with the admission of light and air to the peritoneum, is apparently sufficient to bring about a cure. Vautrin recommends the Pfannenstiel incision for these cases. After evacuation, the ascites may reform in the first few days after operation only to be followed by rapid and permanent disappearance of the fluid.

In addition to laparotomy, Desplas and his associates advocate direct exposure of the lesions to the mercury-vapor lamp for a period of five to ten minutes at 1.0-1.5 meters while the abdomen is open. Postoperatively they radiate their patients twice weekly with a dose which will not cause a temperature elevation of one degree three hours after the exposure and the erythema of which will have disappeared by the time the next séance is due.

In children before the age of puberty the adnexa should be conserved to avoid jeopardizing the subsequent general development of the organism. Nevertheless, Bouilly and Patel advise extirpation of the adnexa even in these cases, as they are convinced that the majority of tuberculous peritonitides in females are secondary to tuberculosis of the fallopian tubes. There is no doubt that many of these cases which have apparently healed are followed by dysmenorrhea, menstrual irregularities, and sterility as the result of dystrophic changes in the ovaries and peritubal adhesions. Sireday maintains that certain examples of obesity, cold extremities, and sterility seen in later life and attributed to endocrine dystrophies can be traced back to a tuberculous peritonitis or Bouilly's "essential ascites of young girls."

Finally, a certain number of cases of fibroplastic tuberculous peritonitis, in which the intestines are intimately bound together with adhesions and in which the genitalia appear as an ulcerocaseous mass that is clearly inoperable, will undergo a remarkable amount of regression after laparotomy and drainage of accessible purulent collections. In this type of case, however, more or less extensive extirpation of the diseased tissue is usually required to bring about a cure.

When the fallopian tubes are grossly tuberculous, the surgeon has no alternative in most cases but to remove them. Unilateral salpingectomy in such cases is extremely hazardous because the disease can be shown microscopically to be bilateral in at least nine-tenths of the cases, even

though one tube appears normal. According to Vautrin, unilateral salpingectomy is indicated only in the rare cases of tuberculous hydrosalpinx which are limited to one side. He has never seen a case of unilateral cold abscess of the tube. To this single indication for unilateral salpingectomy must be added those cases in which a pregnancy is ardently desired and in which the patient has been warned of the very real danger of recurrence.

As a matter of fact, pregnancy following even the most conservative operations in pelvic tuberculosis is very rare and we have been able to find references to only 8 such cases in the literature (Olivier, Macnaughton, Jones, Tedenat, Heully, Muret, Fröhinsholz, and Potvin). According to Fröhinsholz and Feuillade uteroadnexal tuberculosis and pregnancy can develop simultaneously, but such instances must be very rare. There is, however, no doubt that pregnancy may supervene, even in the presence of a diseased uterus, and certain patients may be sufficiently desirous of having children to be willing to take the chance of a second operation.

If a bilateral salpingectomy with removal of the ovaries has been necessitated by extensive adnexal disease, there is no particular value in leaving the uterus in situ. A wish to preserve the menstrual function in young girls in whom an ovary can also be saved is an argument frequently advanced for preservation of the uterus, but it is an open question whether the 50 per cent chance of leaving a diseased organ does not outweigh such a desire.

It has been shown by Rendon and Daniel that the danger of producing untoward symptoms of a surgical menopause in young women by the removal of the ovaries in tuberculous adnexitis is less than in other types of pelvic disease because the internal secretions of the ovary have been so suppressed by toxemia that their removal gives rise to but very few symptoms.

The results of conservative operative procedures collected from various sources are given in Table I.

TABLE I. RESULTS OF CONSERVATIVE OPERATIONS ON PELVIC TUBERCULOSIS

AUTHOR	NO. CASES	L AND W	IMPROVED	RECURRED	DEAD	LOST
Olivier	22				22 %	
Labhardt	41				46 %	
S. Wolff	9				45 %	
Vautrin	14	100 %				
Villard*	6	66 %	33%			
Patel and Olivier†	14	35.7%		7.1%	7.1%	
Potvin‡	3	66 %	33%			
Peterson‡	12	50 %				
Vautrin‡	34	53 %			2.9%	2.08%

*Cited by Condomin; †Unilateral salpingectomy only; ‡Exploratory laparotomy only.

An analysis of the 155 cases listed above shows that 62 per cent of the patients with pelvic tuberculosis subjected to conservative operative procedures are living and have been apparently cured of their affection and that 24.6 per cent are dead. While it is difficult to evaluate this information accurately because in many cases the condition of the patient at the time of operation may have been such that more radical procedures were prohibited, it will be seen that there is actually a greater salvage in the cases in which only an exploratory laparotomy was done than among the patients of Patel and Olivier in whom the tubes were also removed through choice.

A great number of surgeons favor the more radical operation of complete removal of all the pelvic organs in tuberculosis of the internal genitalia. The guiding principle of this group is to attempt to extirpate completely a tuberculous focus which they consider to be primary in many cases and localized to the uterus and oviducts. Such a viewpoint would seem to be commendable in the majority of instances when one considers the frequency with which tuberculous salpingitis is bilateral and that probably more than 50 per cent are associated with tuberculosis of the uterus.

Daniel contends that total castration gives more constant cures because: (a) the convalescence is shorter, (b) the troubles of the artificial menopause, although accentuated in castration for common inflammations, are greatly attenuated in tuberculous cases because the women are frequently amenorrhoeic before the operation, (c) it avoids later operations, necessitated by the existence of a certain number of observations in which the tuberculosis spread to the adnexa left in place after unilateral castration.

According to the same author, the extent of the genitoperitoneal lesions and the gravity of the general condition do not constitute a contraindication to the more radical procedures. "In fact," he says, "the operative danger is not due to the operation itself but to the disease, the principal factor of gravity being constituted by the intestinal wounds upon which the immediate operative prognosis depends."

An analysis of the 961 cases of radical operation collected from the literature shows a salvage of 72.2 per cent for the entire series and a total mortality of 22.6 per cent. The primary mortality of 9.2 per cent compares very well with that reported by Greenhill for operations in which the uterus and adnexa, most of which were inflamed, thickened, and adherent to nearby structures and organs, were removed for non-tuberculous conditions at the Cook County Hospital.

When one considers the end-results obtained by conservative and radical surgery in tuberculosis of the internal genital organs, it is evident that the salvage after the radical procedures is at least 10 per cent greater and the total mortality somewhat less than that following the more conservative operations.

In properly selected cases, the difficulties and dangers in the surgery of pelvic tuberculosis arise almost entirely from injury to the intestines and bladder during the operation. Unlike the adherences encountered in gonorrheal and puerperal inflammations, no line of cleavage is found in tuberculous cases and the intestinal and bladder walls themselves are invaded by the granulation tissue. The separation of these bands may result in perforation of the viscus even though the greatest care be used. In Greenberg's series of 200 cases, complications arose during the operation in 14.5 per cent. Of 104 cases drained, 17.3 per cent developed fecal fistulas. None of the cases without drainage developed this complication. Urinary fistulas occurred in 2.5 per cent and supuration of the incision was recorded in one third.

Although modern methods of anesthesia do not prohibit surgery in cases with coexisting pulmonary tuberculosis, the mortality among this group is distinctly higher than among those in whom the lungs are clear or the pulmonary lesions inactive. According to Greenberg the mortality among patients with pulmonary tuberculosis was 15.5 per cent after operation as compared with a figure of 5 per cent for those without coexisting lung disease.

Peritoneal involvement, except in cases with a few scattered tubercles on the pelvic peritoneum, also increases the hazards of surgery in genital tuberculosis and Greenberg noted an operative mortality in this group of 11.1 per cent as compared to 2.7 per cent for cases without peritoneal tuberculosis.

As the diagnosis of internal genital tuberculosis is usually presumptive until the tissues are actually inspected or examined microscopically, abdominal section must remain the method of choice of attacking the disease surgically. It is only when the abdomen has been opened that the extent of the involvement can be estimated and the complicating factors visualized. The entire peritoneum can then be exposed to light and air and conservative or radical measures carried out according to the indications. In addition, it not infrequently happens that apparently inoperable lesions are found at laparotomy to be less extensive and more amenable to treatment than was suspected preoperatively, a fact that has been repeatedly emphasized by Lecene, Pollosson, and Daniel. Because of the factors noted above, vaginal operations have never been popular in pelvic tuberculosis.

Löhlein, Turner, and Wetterdal have recommended posterior colpotomy for diagnosis and treatment in genitoperitoneal tuberculosis. Through such an incision Löhlein and Turner claim to have removed tuberculous adnexa as completely as by the abdominal route, but most authors who employ posterior colpotomy do so for diagnosis or drainage of obvious culdesac abscesses presenting behind the cervix. In several

cases Wetterdal has been able to establish the diagnosis of tuberculosis by material obtained from such a puncture or by actual palpation of the lesions through the incision.

On the other hand, the procedure is not without serious objections in tuberculous cases. The seriousness of implanting a secondary infection on a tuberculous process is well recognized, and when culdesac drainage is employed, it is very apt to give rise to permanent fistulas. We have had an opportunity of observing an instance in which the procedure in a tuberculous patient resulted in a perforation of a closely adherent loop of the colon and was followed by death of the patient.

Roentgen therapy for peritoneal and genital tuberculosis was introduced by Bircher in 1908, but it is only recently that the measure has attracted the attention it merits. Among the many reports favoring this type of therapy—alone or combined with conservative surgery—may be mentioned those of Beclere, Gibert, Keller, Edling, and Violet in France; Krönig, Gauss, Bumm, Menge, Kermauner, Zweifel, Fuhrmann, Baer, Schumacher, Bircher, Siedentopf, Seisser, and Hörnicke in Germany; Schauta in Vienna; B. Solomons in Ireland; Cuzzi and Pestalozza in Italy; and Ford, Kolischer, and Polak in the United States.

Since Bircher's original paper, the indications for x-ray treatment have been extended by certain of its enthusiastic advocates to include all types of pelvic tuberculosis. They point out that radiotherapy is attended by no immediate mortality and is not contraindicated by the gravity or extent of the lesions. Even in those cases in which excision seems justifiable, Martius, Gibert, and others are emphatic in stating that operation should never be done until a course of radiotherapy has been tried. It is claimed that this line of conduct will avoid all intervention in some cases, but more often it will result in at least a partial sterilization of the focus and an arrest in the extension of the lesions so that the danger of operation to remove residual foci or collections, against which the x-ray is powerless, is diminished.

As with the surgical treatment, two schools have arisen among those favoring irradiation of pelvic and abdominal tuberculosis. The method of small doses, which endeavors to avoid castration, is advocated by the majority of workers and has undergone considerable development in Germany. Proponents of heavy doses with resulting permanent castration defend their stand by pointing out (1) that it is impossible to fix a dose for temporary castration and (2) even if it is successfully attained it is undesirable because the congestion at the menses favors reactivation of the pelvic tuberculosis; (3) in women cured of adnexal tuberculosis the chances of becoming impregnated and of going to full term are minimal; (4) the adhesions, stenoses, and tortuosity of the tubes in cured cases predispose to extrauterine gestations; and (5) the ova in irradiated ovaries are probably weakened, abnormal, and unhealthy.

Still others, such as Edling, Weibel, Pestalozza, and Gibert, believe that roentgen therapy finds its greatest indications as a postoperative measure following conservative or radical surgery. According to this group, it is not a question of the x-rays versus surgery but of an association between the two. By following this regime, Edling's cures have risen from 66 per cent to 87 per cent.

X-ray therapy also appears to have a useful field in the treatment of postoperative tuberculous fistulas. Gibert has reported a case of a girl in whom a fistula developed in the cicatrix fifteen years after a laparotomy for tuberculous peritonitis. Examination showed an opening which discharged pus in the intermenstrual period and blood during the menses and which was associated with a small hard juxtauterine mass. X-rays were administered, the fistula closed, and follow-up eighteen months later showed a perfect result.

It is beyond the province of this report to detail the various technics now in use for the administration of roentgen therapy in pelvic tuberculosis. Suffice it that those who favor the smaller doses employ $\frac{1}{25}$ to $\frac{1}{10}$ H.E.D. at a focal distance of 35-50 cm. with rather heavy filters of copper, aluminum, or zinc. The treatments are given at rather long intervals and repeated as necessary to bring about a cure. The proponents of large dosage use technics similar to those commonly employed in malignancies of the pelvic organs.

The results of small doses of x-rays in pelvic tuberculosis are tabulated in Table II.

TABLE II. RESULTS OF SMALL DOSES OF X-RAYS IN PELVIC TUBERCULOSIS

AUTHOR	NO. CASES	APPARENTLY CURED	IMPROVED	DEAD
Keller	10		90%	10%
Vogt*	14	43%	21.4%	14.3%
Muller†				8%
Uter	24	87.5%	8.3%	
Polak	2		100%	
Ford			66%	
Edling	102	55%	40.2%	3.9%
Schumacher			70-80%	
Sippel	17	58.8%	17.6%	

*Cited by Edling; † Cited by Wetterdal.

Because of the difficulty in obtaining proof of a cure, it would be unjustifiable to draw conclusions from this series of 169 cases treated with small doses of x-rays that could be compared with the figures obtained with surgery. Suffice it, therefore, to indicate that 82.8 per cent showed definite improvement under this regime, and one may assume that many of them went on to complete healing. The recorded mortality averaged 9 per cent.

Unfortunately, no figures are available for series in which large doses of irradiation were used that can be compared with those given in Table II, for small doses. In 17 proved cases treated by Gibert and followed

one to four years, 11 had submitted to previous laparotomies with or without removal of tissue and 6 had had no surgery before the radiation was administered. Of this group of 17 patients, 3 are dead of progression of their tuberculosis, 5 are considerably improved but cannot be considered cured, and 9 are perfectly well.

The 2 patients treated by Violet were not controlled by laboratory diagnosis; both were successfully treated in spite of the presence of fistulas.

TABLE III—STATISTICS ON COMBINED X-RAY AND SURGERY

AUTHOR	NO. CASES	APPARENTLY CURED	IMPROVED	WORSE	DEAD
Stephan*		77%			
Vogt*		70%			
Edling	53	64.1%	30%		5.7%
Wetterdal	16			12.5%	

*Cited by Wetterdal.

Wetterdal, Edling, and others have advocated surgery followed by x-rays in the treatment of tuberculosis of the pelvis and have published encouraging accounts of the results obtained. However, sufficient data have not yet accumulated to warrant intelligent comparison with the other measures now in use. Table III shows the results obtained in reports published to date.

We have had opportunity to observe 2 cases of pelvic tuberculosis upon which x-rays have been used. The protocols are given below:

CASE 1.—F. M., aged forty-one years, single. Patient with pulmonary tuberculosis, Stage III, was seen April 24, 1931, for profuse uterine bleeding. Present attack has lasted three weeks and is accompanied by pain in the lumbar region and groin. There were no menses during January and February of this year. She gave a history of more or less similar attacks all her life, and irregular menstruation. A uterine suspension was done sixteen years ago for the bleeding; seven years ago she bled continuously for six months and was then curetted. The pain began four years ago, about the time she began pneumothorax therapy. She has far advanced pulmonary tuberculosis with cavitation. Artificial pneumothorax was started four years ago with considerable improvement to date.

Physical examination showed a well-nourished and developed white female. The examination of the abdomen was negative. The external genitalia were not remarkable. There was some pouting of the external urinary meatus. The vagina contained blood. The cervix was small, firm, and freely movable. The uterus was slightly larger than normal with a firm round protuberance the size of a walnut in the region of the left cornua. The adnexa were negative.

Examination of the urine showed no abnormalities. The blood count was as follows: Hemoglobin (Sahli) 75 per cent, R.B.C. 4,830,000, W.B.C. 11,400, polymorphonuclears 65 per cent, lymphocytes 24 per cent, monocytes, 3 per cent, eosinophiles 4 per cent, basophiles 2 per cent, transitional cells 2 per cent.

On April 27 a diagnostic curettage was done at which a rather excessive amount of endometrial tissue was obtained. On curetting the left cornu a peculiar grating sensation was felt through the curettes, and the tissue obtained from that portion was noted to be granular in character. The tissue was divided into two parts, one of which was submitted to microscopic examination and the

other was inoculated into two guinea pigs. The histologic examination was inconclusive; no tubercles were found but a single typical giant cell was found. Both guinea pigs died of generalized tuberculosis.

The patient was given roentgen radiation treatments beginning May 1, 1931. On June 23, 1931, the patient reported two menstrual periods since operation which were profuse and accompanied by severe pain. She had had eight treatments and did not wish to continue because of her general malaise. The treatments, however, were continued and on August 4 she reported amenorrhea since June, no bleeding or pain. There was no gain in weight. She stated that she felt better than she had for two years. At that date she had had nine treatments. Examination showed no pigmentation of the abdomen. The vaginal examination showed some contraction of the vagina; the uterus was somewhat fixed and slightly tender. A check-up on Nov. 13, 1932, found the patient in good health since her last visit except for a profuse irritating leucorrhea and slight spotting on one occasion. Examination of the abdomen was negative. Pelvic examination showed considerable reddening and inflammation of the vagina with negative findings as far as the internal genitalia were concerned. The vaginitis cleared after the use of green soap and bichloride douches.

On Nov. 21 reexamination showed some definite tenderness of the uterus, especially in the left cornual region. A smear of the vaginal secretion was negative for acid-fast bacilli.

CASE 2.—M. G., aged twenty-six years, divorced. Patient was seen April 8, 1932, for lower abdominal pain of three days' duration. She had a generalized pulmonary tuberculosis and had had artificial pneumothorax treatment for some time. The abdominal pain was localized to the suprapubic region. There were no bladder symptoms. Patient was operated upon for a left ectopic pregnancy in 1923 at which time the left tube was removed. In 1930 she was again operated upon for a supposed ovarian cyst which proved to be a right tuberculous tubo-ovarian lesion and was removed. The uterus appeared normal at that time.

Physical examination showed a fairly well-nourished and developed adult white female. The abdomen was very tender suprapubically. Inguinal adenopathy was noted. The external genitalia were not remarkable. The cervix was clean. The uterus was small, A.F. and A.V. and very tender. The fornices were clear.

On the basis of the right tuberculous salpingitis for which she had been operated upon two years before and the absence of any sexual history since that date, a diagnosis of tuberculosis of the uterus was made. A diagnostic curettage was not done for financial reasons.

The patient was given x-ray treatments. On July 8, a check-up after eight treatments was made. The patient reported that until the last two treatments she was relieved of her pain for four days after each radiation; since then she has had no pain at all. Examination showed a very small, nontender uterus which was freely movable. It was decided to give her a month's rest from treatments.

On September 16, the patient reported that she had gained seven pounds and felt very well until two weeks ago when she began to have some abdominal pain after meals and diarrhea; there has been some frequency of urination, pain in the lumbar region, fever, and general debility. Blood sedimentation: 28 mm. Examination showed the uterus smaller than before, A.F. and A.V. and freely movable.

She was seen in October, 1932, and found to be in good condition.

In January, 1933, there was a return of the frequency of urination, urgency, dysuria, pain in the costovertebral angle, especially on the right side and in the

right lower quadrant. She had lost five pounds in the last four weeks. The pelvic examination was negative. The vaginal secretion contained no acid-fast organisms. Catheterized specimens of urine showed no tubercle bacilli on two occasions; a guinea pig was inoculated but no report has been received to date.*

Both of these patients are free from pelvic symptoms at the present time (Dec. 6, 1933). They are employed on part-time work although the general tuberculous condition is unimproved.

COMMENT

An attempt has been made in this report to evaluate the results of our present methods of treating tuberculosis of the internal genital organs. That they are not satisfactory is evident and the necessity of regarding genital tuberculosis as a very serious condition is apparent. Unlike the common gonorrheal and puerperal inflammations of the tubes and uterus, in which the treatment is concluded when the diseased tissues have been removed, tuberculosis of the parts is but a local manifestation of a general condition and the treatment is never complete until the infection has been brought under control by the use of those measures that have been found efficacious in the treatment of tuberculosis elsewhere in the body.

There is urgent need of greater care in the diagnosis of the etiology of pelvic inflammatory conditions. A routine hit-or-miss section through an inflamed tube for microscopic examination is not sufficient if the best interests of the patient are to be observed. It has been said that in one case von Franqué examined 265 sections before encountering a typical tuberculous lesion. This may seem absurd but a recognition of the true nature of the condition is essential. The value of guinea pig inoculation is demonstrated in the first case cited above and the test should be made at least in every patient with evidence of tuberculosis elsewhere in the body.

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*No regular routine was followed in the treatments given above. The dosages were regulated by the condition of the patient. The apparatus available was unable to deliver a high voltage such as is used in most deep x-ray therapy and the nine-inch spark gap corresponds to about 110 K. V. The erythema dose equals 7 minutes—42 seconds.

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6 CHURCH STREET

PATHOLOGY OF INTRACRANIAL HEMORRHAGE IN THE NEWBORN CHILD

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THE problem of intracranial hemorrhage in the newborn has always been one of great interest to the obstetrician. In 1667, Willis,¹ the great English physician, first described the disease, and since that time numerous authors have discussed its mechanism and the possible measures for its prevention.

In 1862, Little called the attention of pediatricians to the subject by asserting that intracranial hemorrhage at birth is the cause of most of the spastic paralyses of later childhood. After him, many writers tried to prove that nearly every mental or neurologic deficiency in children is caused by a brain injury at birth, and the obstetrician was exposed to the criticism of the entire medical world. For instance, in 1930, Peterman² made the following statement: "Intracranial hemorrhage is responsible for most of the convulsions which occur in the first year, and for almost all the hemiplegias, diplegias, and paralysis found in childhood. The conclusions to be drawn from the result of intracranial hemorrhage in the newborn must be offered to the obstetrician."

The pathologists of the old school of morphology (Virchow, Kundrat) were satisfied with the autopsy findings and the publication of the few statistics compiled from these findings. Beneke³ (1910) was one of the first pathologists to attempt to investigate the mechanism of intracranial hemorrhage in the newborn, and his method and findings are still considered to be of outstanding importance. It was his method of opening the skull which gave us for the first time an exact picture of the pathology of birth trauma.

Ehrenfest⁴ proposed to discard all old pathologic reports because they "often express nothing but mere surmise and theory." His monograph, *Birth Injuries of the Child*, includes a thorough résumé of the pathology and symptomatology of intracranial hemorrhage in the newborn, with numerous statistics and a critical review of the literature up to 1930. He cites the following important facts as "irrefutably established: (1) Intracranial traumatic lesions, light and severe, develop in the course of both normal and abnormal labor. (2) Evidence of such injuries can be discovered at autopsy in approximately one-half of all infants, stillborn or dying within the first few days of life."

The statistics, regarding the frequency of intracranial hemorrhage in the newborn, which appear in the literature are so varied that a comparison is hardly possible. One reason for this is that each author follows a different statistical method. For instance, Henschen⁵ found in 1,277 autopsies of infants that death was due to brain hemorrhage in only 29 cases, or 2.27 per cent. Schwartz,⁶ on the other hand, observed indications of hemorrhage in the brains of 105 out of 110 stillborn infants. It is evident that the results obtained by these two authors cannot be compared, since Henschen⁵ recorded only hemorrhages of the brain which he believed to be the cause of death. Schwartz,⁶ however, counted each microscopic hemorrhage which he found in the brains of the stillborn infants. Even if we allow for the difference in compiling statistics, there is still much confusion because of the difficulty in interpreting the terms used. The differentiation between living and stillborn infants, between viable and nonviable stillborn infants is arbitrary. Autopsies are usually done in the routine manner by some one who is not especially interested in this problem. Small hemorrhages and lacerations of the tentorium are often overlooked, or on the other hand, are produced during the autopsy by rough handling of the infant's head. The decision as to whether the hemorrhage was the cause of death is difficult if the blood clot is small. Very often localization of the vessel injury is impossible. These various factors are not always noticed in the course of routine technic or are overlooked in the publication of the compiled statistics, especially if the autopsy material is put at the disposal of the pediatrician or the obstetrician, who is not in a position to know all the possibilities of error in the autopsy protocol.

It has been shown repeatedly that symptoms of intracranial hemorrhage can be produced by the presence of other diseases. The finding of blood in the spinal fluid is a very good lead for a diagnosis but is not reliable (Lippman,⁷ Grulee,⁸ Ford,⁹ and Levinson.¹⁰).

Glaser¹¹ reported the finding of blood in the cerebrospinal fluid in only 19 out of 26 cases of intracranial hemorrhage, and in 13 of his 42 control cases. He considers the presence of erythrocytes in the spinal fluid to be a physiologic occurrence. In Sharpe's¹² examination of 400 infants, blood was found in the spinal fluid in 45 out of 73 cases in which clinical symptoms of hemorrhage were present. Only three of these infants died from massive brain hemorrhage.

In a case of intracranial hemorrhage in an infant born alive or dead, a careful autopsy is absolutely necessary, if an exact picture of the pathologic condition is to be secured.

In our hospital, the technic of an autopsy of the skull of an infant is as follows: A small window is cut in both parietal bones, as suggested by Meyer and Hauch,¹³ in order to rule out the presence of blood on the convex side of the brain, and of injuries to the superior

cerebral veins which open into the sagittal sinus. The autopsy is then continued by the method of Beneke and Zausch.¹⁴ Both hemispheres of the brain are taken out carefully with the fingers, and the tentorium, the falx and the brain stem with the vena magna (galeni) exposed. Through two small windows in the tentorium the subtentorial space and the cerebellum are inspected and the latter removed. When a hemorrhage is present, the blood clot is carefully removed with a forceps, and the vessels of this region are exposed. Sometimes it is almost impossible to discover the injured vessel. Previous hardening of the skull in formalin is recommended, but is not absolutely necessary. To determine whether the infant is mature or premature, the method of Chase¹⁵ in which he compares the length and weight of the infant body with the clinical evidence as indicated by the menstrual history of the mother, has proved most successful. The diagnosis of stillborn infant is taken from the chart of the infant since the pathologic methods of diagnosis can be as erroneous as the clinical. For the same reason no differentiation between viable and nonviable stillborn infants is made.

The autopsy is followed by a microscopic examination of all the organs of the body, in order to determine whether any other disease is present which might be an etiologic factor in the occurrence of the hemorrhage. Hemorrhagic child disease and congenital syphilis are easily diagnosed at the autopsy table, and their presence may be confirmed by microscopic examination. Intrauterine asphyxiation is diagnosed by the presence of amniotic fluid in the alveoli of the lung.

The statistics reported in this paper are taken from our findings from autopsies of 317 full-term and premature infants. Two hundred and fifty-four infants lived for a short time after birth. Sixty-three were recorded as stillborn. In 50 cases, or 16 per cent of our total number of cases, an intracranial hemorrhage was found at autopsy. In Table I the incidence of intracranial hemorrhage in the newborn as compared with the birth rate at the Charity Hospital for the years 1931 and 1932 is shown.

TABLE I

	1931		1932	
Infants born alive		2,395		3,112
Brain hemorrhage diagnosed clinically	10		9	
Brain hemorrhage discovered at autopsy	17		25	
Total	27	1.13%	34	1.09%

These figures are in accord with more extensive statistics in the literature in which the mortality from intracranial hemorrhage in the newborn is given as from 1 to 2 per cent.

Table II shows the frequency of hemorrhagic lesions found at autopsy in our series of 50 cases of intracranial hemorrhage in the infant. The material is grouped after the suggestion of Chase.¹⁵ We avoided the differentiation of viable stillborn and living infants for the reason previously mentioned.

TABLE II

PATHOLOGIC FINDINGS	PREMATURE INFANTS	FULL-TERM INFANTS	TOTAL
1. Large supra- or infratentorial hemorrhage with laceration of the tentorium	11	11	22—44%
2. Large subdural hemorrhage on the convex side of the brain with possible injury to the sagittal sinuses and superior cerebral veins	10	2	12—24%
3. Small subdural hemorrhages without apparent vessel injury	5	7	12—24%
4. Intracerebral hemorrhage	1	3	4—8%

As will be noted from Table II, by far the largest number of cases showed the pathologic picture of Group I (44 per cent). Its frequency is equally divided between full-term and premature infants. The predominance of the pathologic findings of Group II among premature infants is remarkable.

Table III presents some of the factors brought out in the history or at autopsy in our cases which, according to the literature, are important in the etiology of intracranial hemorrhage in the newborn infant.

TABLE III

POSSIBLE ETIOLOGIC FACTOR AS REVEALED BY HISTORY AND FURTHER EXAMINATION	PREMATURE INFANTS	FULL-TERM INFANTS	TOTAL
Labors in which the history or course suggests or proves the presence of factors, chiefly mechanical, likely to lead to damage	16	13	29
Asphyxia diagnosed at autopsy	2	5	7
Diseases of the newborn: congenital syphilis, hemorrhagic disease	9	5	14
Diseases of the mother: typhoid, tuberculosis, eclampsia	2	1	3
Normal spontaneous delivery	12	2	14

In 48 per cent, or nearly half of our cases, birth trauma is recorded in the history. The term "birth trauma" is understood to include all factors, chiefly mechanical, which are likely to lead to damage in the course of labor (Ehrenfest). Atypical positions, as face presentation; breech position; surgical deliveries, as high, middle, and low forceps; version; extraction; an abnormally long period of labor, or the abuse of pituitrin, represent the circumstances in which the fetus is more exposed to trauma during delivery than in a normal birth. The fact that nearly half of our autopsy material shows the incidence of one or more factors which may cause trauma is significant. We shall not discuss individually the factors mentioned above, because we feel that

the number of cases represented in each group is too small to avoid gross statistical errors. Sixteen living or stillborn infants which were exposed to trauma during delivery were premature; 13 were mature at the time of birth. Congenital syphilis and hemorrhagic disease of the newborn, which are considered by some authors as important factors in intracranial hemorrhage, were recorded in 14 instances or 28 per cent of our autopsies. In three cases or 6 per cent, a severe disease was present in the mother. Seven cases or 14 per cent showed the microscopic picture of intrauterine asphyxia. The lung alveoli were partly compressed and contained amniotic fluid. Fourteen cases, or 28 per cent, showed that labor had been normal and the examination of the body of the infant revealed no disease which might account for the occurrence of intracranial hemorrhage. Twelve of these infants were prematurely born. In nine cases there was a laceration of the tentorium or a massive hemorrhage with injury of the longitudinal sinus.

DISCUSSION

Ehrenfest⁴ classifies the pathologic conditions found in cases of intracranial hemorrhage as follows:

- (1) Cephalhematoma internum
- (2) Subarachnoidal hemorrhage
- (3) Dural hematoma
 - (a) Supratentorial
 - (b) Infratentorial
 - (c) Mixed types
- (4) Brain hemorrhage
 - (a) Ventricular
 - (b) Diffuse or circumscribed

He considers cephalhematoma internum and subarachnoidal hemorrhage to be of less importance than dural hematoma.

From the pathologic-morphologic point of view, the classification of Ehrenfest⁴ does not seem to be adequate as it does not cover all pathologic possibilities, even if we have to concede that it is a very good aid in interpreting their origin and in diagnosis. The following suggested classification is an attempt to express more definitely the location of the hemorrhage.

- (1) Epidural hemorrhage or epidural hematoma
- (2) Intradural hemorrhage or intradural hematoma
- (3) Subdural hemorrhage or subdural hematoma
- (4) Subarachnoidal hemorrhage
- (5) Subpial hemorrhage
- (6) Intracerebral hemorrhage

Epidural hemorrhage, or cephalhematoma internum, is rarely found in the infant. It occurs practically only in combination with severe injury to the skeleton of the skull and may be of venous or arterial origin. *Intradural hemorrhage* may be found

in cases of asphyxia and hemorrhagic child disease. The hemorrhage is usually of slight extent and is of no clinical importance. There are only two types of intradural hemorrhage which may become so large as to endanger the life of the infant, namely, the intratentorial hemorrhage and the hemorrhage occurring between the two folds of the falx cerebri at the root of the falx. *Subdural hemorrhages* may be subdivided according to their location into supratentorial, infratentorial, and hemorrhages filling the subdural space on the convex side of the brain. The subdural hematoma is very often associated with a more or less severe injury of the dura, the most common type of which is rupture of the tentorium. As emphasized by many authors, the tentorium ruptures most easily on its free margin near the root of the falx. Sometimes a small rupture in the neighborhood of the straight sinus may lead to profuse bleeding. Smaller hemorrhages into the supratentorial or infratentorial space may be produced by injury to small intratentorial veins. Not all supratentorial hemorrhages have as origin a laceration of the tentorium. Injury to the vena magna may produce the same picture. Injuries of the sagittal sinus and of the superior cerebral vein (Ehrenfest) lead to profuse hemorrhage on the convex side of the brain which very often extends into the subarachnoidal space. Small *subarachnoidal hemorrhages* with subdural hematoma are believed to be of rather common occurrence in the newborn (Ehrenfest). They are listed in our material in Group 3, Table II, and comprise 24 per cent of our reported cases. Usually syphilis or hemorrhagic disease of the newborn is found in these cases and premature infants seem more disposed than the mature newborn. *Subpial hemorrhage* has been described by Schwartz,⁶ Wohlwill,¹⁶ Siegmund,¹⁷ Joel,¹⁸ Hemsath and Canavan¹⁹ and others. Glaser¹¹ found no blood in the cerebrospinal fluid in nine cases of subpial hemorrhage. Hemsath and Canavan¹⁹ show convincing pictures of small subpial hemorrhages which are associated with small blood extravasations into the brain.

In contrast to the other groups mentioned above, larger, macroscopic *intracerebral hemorrhage* is rather rare in the newborn. The soft brain of the premature infant seems to be more disposed to this type of hemorrhage than the brain of the full-term newborn (Couvellaire). Only 4 of our 50 cases presented a macroscopically visible intracerebral hemorrhage. In contrast to this finding may be cited some recent neurohistologic reports from the literature. In a microscopic examination of 110 stillborn infants, Schwartz⁶ found small hemorrhages in 105 cases. Joel¹⁸ studied the significance of the fat globule cell which is found sometimes in large numbers in the brain of the newborn infant (Virchow's encephalitis neonatorum), and denies its pathologic importance. Hemsath¹⁹ found microscopic hemorrhages in 34 out of 53 autopsied cases. In 12 cases no other cause of death could be found. Crothers²⁰ emphasizes the importance of minute hemorrhages in the medulla of the newborn as a cause of asphyxia. Grulee⁸ is right when he states that the obstetrician is in no position to make a diagnosis in the majority of instances of microscopic intracerebral hemorrhage. Lande²¹ warns against overemphasis on the possibility that the occurrence of small hemorrhages during birth may be a factor in neurologic diseases in later life. The significance of small degenerative foci in the brains of infants is still being discussed (Jastrowitz,²² Birsch-Hirschfeld, Fischl,²³ Ceelen,²⁴ Schmincke,²⁵ Schwartz,⁶ Harbitz,²⁶ and others). According to Siegmund,¹⁷ the conception, "Encephalitis congenita," should be abandoned (Kaufmann²⁷).

The autopsy findings in our reported cases were all typical and easily recognized. The extravasated blood was almost always of a dark red color and showed no or few signs of organization. In all our cases the spinal fluid was markedly reddish in color and had a

hazy appearance. Sometimes unclotted blood was found in the skull. We shall discuss the significance of this finding later on. A traumatic lesion could be observed in most of our subtentorial and supratentorial types. Passive congestion of the cerebral veins was present in about half of our cases. In those cases also a more or less severe cyanosis of the skin and passive congestion of the organs could be noted.

The diagnosis of asphyxia was made by the obstetrician in a great many cases. In those live born or stillborn infants, in which we found a single large hemorrhage, the diagnosis of asphyxia had to be discarded and the brain hemorrhage regarded as the cause of death. Yagi²⁸ divided asphyctic conditions of the newborn into two groups, namely, asphyxia suffocatoria and asphyxia apoplectica. The latter is the result of compression of the medulla by a large brain hemorrhage. In our series of 50 cases, a diagnosis of primary intrauterine asphyxia could be made in only seven cases, or 14 per cent. The diagnosis is difficult but from the size of the hemorrhage and the appearance of the clotted blood it is often possible to make a differential diagnosis. The presence of unclotted blood is more suggestive of asphyxia suffocatoria. The hemorrhagic lesions in this condition are not very extensive and are usually multiple. A marked passive congestion of the brain vessels usually accompanies the asphyctic brain hemorrhage, a condition which Cruickshank²⁹ also emphasizes. The picture of the lungs is an aid in the differential diagnosis only when the infant is born alive. The presence of congenital syphilis and hemorrhagic child disease may be easily determined by microscopic examination. Usually bleeding from the nose or from the umbilical cord is a factor in the history, or large hemorrhagic effusions may be found in the pleura or in the peritoneum. In view of the above considerations, we did not find it difficult to separate the picture of spontaneous intracranial hemorrhage of the newborn from similar conditions caused by asphyxia, congenital syphilis, or hemorrhagic child disease.

ETIOLOGY

Intracranial hemorrhage in the living and stillborn infant is undoubtedly of a purely mechanical nature. In the majority of cases, atypical position, difficult labor, and surgical delivery are recorded in the history of the mother. According to Kuhn,³⁰ the incidence of intracranial hemorrhage is ten times as great among infants delivered surgically as among those delivered spontaneously. Heidler³¹ reports that in 65 out of 131 cases of ruptured tentorium with massive supra- or infratentorial hemorrhage, version with extraction has been performed. Becker³² found a history of difficult and prolonged labor in 100 per cent of his cases of intracranial hemorrhage. Seventy-five per cent of these infants were firstborn. Chase¹⁵ states that in half of his cases of subdural hematoma the infants were delivered surgically. Croth-

ers²⁰ found large intracranial hemorrhages with tears of the tentorium in 88 per cent of his cases of premature infants delivered surgically. In 48 per cent of our cases there was a history of birth^{*} traumatization. Beneke³ stressed the mechanical etiology of the injury of the tentorium as opposed to the asphyxia theory of Seitz.³³

Opinions are divided as to the exact explanation of the mechanism of injury through birth traumatization. Holland,³⁴ like Beneke,³ sees in the molding of the infantile head and its changes in diameters during its passage through the birth channel, the greatest danger of intracranial injury. One of the functions of the dura is to hold the loose skeleton of the infantile skull together and to prevent exaggerated disfigurements. This function is performed mainly by the two processes of the dura which are formed by folding of the inner layer, the tentorium, and the falx. Changes in the diameters of the skull exert a pulling effect on both membranes which may cause a rupture. This may occur if the stretching or the compression of the infantile skull is abnormally great as seen in instances of great disproportion between the infantile head and the birth channel of the mother. The normal process of molding may become endangered if the tentorium and the falx are not sufficiently developed to resist the physiologic strain. Chase¹⁵ stressed the importance of a normally developed tentorium for the prevention of birth injury and his observation has been confirmed by many authors. Prematurity of the infant, therefore, must be regarded as an important factor in rupture of the tentorium through the physiologic molding of the infantile head.

As pointed out by Ehrenfest,⁴ of etiologic importance in a case of subdural hematoma occurring on the convex side of the brain, is the fact that by compression of the infantile skull from the temporal side, an overriding of the parietal bones takes place, and the distance between the dura and the arachnoid of the brain which is crossed by the subdural veins is changed on both sides. Therefore, a rupture of one of those vessels may easily occur. Sachs³⁵ sees, in the springing apart of the parietal bones after the child's head leaves the birth channel, a reason for the occurrence of subdural hematoma on the convex side of the brain. The difference in pressure between the intra-uterine cavity and the vagina is noted, as a cause of intracranial hemorrhage by Seitz,³³ Hannah³⁶ and others. Joel¹⁸ sees a cause for brain hemorrhage even in the sudden rupture of the amnion sac. Schwartz⁶ refers to the experiments of Ylppö³⁷ who could produce small hemorrhages in the skin of the newborn by means of a suction pump. He refers to the fact that no intracranial hemorrhages are found in animals and believes that the sudden change in pressure after the infantile head leaves the uterus is an important factor in brain hemorrhage. Even if we concede that a small hemorrhage in the neighborhood of the soft fontanels might be produced by a change in pressure, it does not

seem likely that this occurrence would be of any etiologic importance in the case of a large intracranial hemorrhage. In the cases reported by Ylppö,³⁷ the hemorrhages were only small subcutaneous hematomas. That intracranial hemorrhage does not occur in animals at birth is due to the fact that the skull is firm, and therefore no mechanical molding can take place. We do not believe that the difference in pressure in the uterus, in the vagina, and after the birth of the child, explains the majority of cases of intracranial trauma at birth.

Intrauterine asphyxia has been emphasized by Seitz³³ and others as a possible cause of brain hemorrhage. Irving³⁸ states that in any case of asphyxia associated with brain hemorrhage, the asphyxia is the primary cause of the hemorrhage. We have demonstrated previously that the differential diagnosis of primary and secondary asphyxia can be made in almost every instance. Ehrenfest⁴ says that the "etiologic relation of asphyxiation to intracerebral parturitional lesions is practically limited to the plausible assumption that a congested sinus or vein is more likely than an empty one to rupture under pressure strain." Modern writers regard asphyxiation only as a predisposing cause or a contributory factor, or as a result of injury to the respiratory center.

Among the diseases of the newborn, congenital syphilis and hemorrhagic child disease are believed to be important factors in the mechanism of intracranial hemorrhage. The modern conception that syphilis is a cause of intracranial hemorrhage is probably true only so far as the condition is responsible for the prematurity of the infant (Ehrenfest, Chase). As previously mentioned, hemorrhagic diathesis can be easily differentiated from spontaneous hemorrhage by the autopsy findings. The former condition is usually the cause of small subarachnoidal hemorrhages which do not endanger the life of the child, but may be the cause of neurologic deficiency in later life (Jackson's epilepsy). Twenty-eight per cent of our cases showed one or both of the conditions mentioned above. A traumatic hemorrhage of the skull is likely to be greater if hemorrhagic diathesis exists, and for this reason the latter must be considered as a very important contributory factor.

All modern statistics regarding cephalic birth injuries point clearly to the etiologic significance of prematurity. Pearson and Wyllie³⁹ quote Brown who never saw a brain hemorrhage in a full-term child after normal delivery. Tyson and Crawford⁴⁰ report the finding of intracranial hemorrhages in 35 full-term and 10 premature infants; all 10 premature infants died from the trauma. King and Loeber⁴¹ emphasize the importance of prenatal study of the fetus for the prevention of intracranial hemorrhage. Chase¹⁵ showed with photomicrographs the great difference between the tentorium of a fully developed infant and that of a premature infant. He points out that prematurity is a most impressive factor in birth injuries. The smaller the child at birth, the greater the frequency of hemorrhage (Capper⁴²).

In our experience also, prematurity was a predisposing factor in 54 per cent of the cases which came to autopsy. In 10 cases prematurity was the only possible explanation for the occurrence of the intracranial hemorrhage, and in these cases the trauma of the normal birth mechanism was sufficient to cause the injury. Beneke,³ Pott,⁴³ Meyer and Hauch,¹³ Ylppö,³⁷ and many others described laceration of the tentorium in premature fetuses delivered quickly and spontaneously. The disposition to tearing and hemorrhage of the undeveloped tentorium is so great that this factor alone may be considered to be a cause of intracranial hemorrhage in many instances.

From the point of view of the pathologist, I wish to emphasize the importance of prematurity as a predisposing factor in the occurrence of intracranial hemorrhage in the newborn. It is my belief that if the incidence of premature births can be decreased, the incidence of intracranial hemorrhage will be greatly reduced. I refer not only to large hematomas but also to the small blood extravasations which often prove fatal in later life.

SUMMARY

From a total of 317 autopsies of full-term and premature infants, 50 cases of intracranial hemorrhage are reported and discussed.

The importance of a careful autopsy technic is stressed in order to avoid errors in statistics.

A new classification of intracranial hemorrhages in the newborn is suggested.

Prematurity as a predisposing factor is emphasized.

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BIRTH INJURY OF THE OCCIPITAL BONE WITH A REPORT OF THIRTY-TWO CASES*

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THIS series of 32 cases of separation of the posterior intraoccipital synchondrosis is reported for the purpose of calling attention to the fragility of the base of the skull in the full-term fetus.

At birth the occipital bone is composed of four segments, the squamous, two lateral, and the basilar portions, separated by cartilage forming the anterior and posterior intraoccipital synchondroses. The posterior synchondrosis has been variously named the occipital hinge¹ and the obstetric joint² because it normally permits a hinge-like motion of the squama during labor. It is also quite vulnerable as a point of injury during labor.

The lateral view roentgenogram of the normal fetal skull, Fig. 1, shows the location of the posterior intraoccipital synchondrosis. Excessive pressure exerted in the suboccipitobregmatic direction may cause internal displacement of the squama and overriding, the dura mater being stripped from the lateral portions and the pericranium from the squama (Figs. 2 and 3). The posterior atlantooccipital ligament, which forms by far the strongest anchorage of the inferior squamous border, may be ruptured or torn from its insertion (Fig. 4). Circulation is obstructed in the occipital sinus and those inferior cerebellar veins which are its tributaries. The overriding decreases the size of the posterior skull fossa and forms a transverse ridge across the floor of the fossa, frequently leaving a corresponding depression on the inferior surface of the cerebellum (Fig. 5). This injury is far more serious than the overriding of the bones of the cranial vault because here the pressure is exerted in close proximity to the respiratory center in the medulla oblongata.

*Read before the Section of Obstetrics and Gynecology, New York Academy of Medicine, March 28, 1933.

Only three cases of this separation, or osteodiastasis, have been reported since the injury was first described by Schroeder³ over sixty

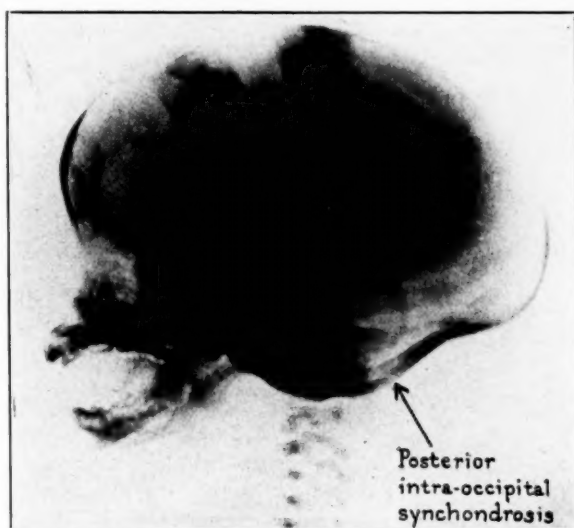


Fig. 1.—Lateral view of fetal skull at term.

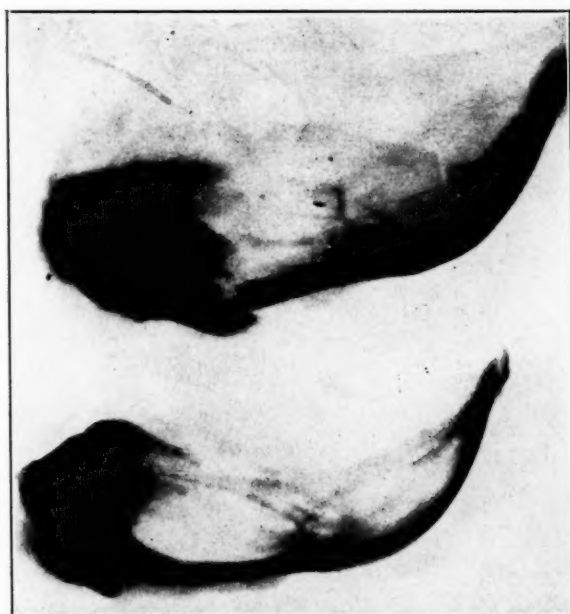


Fig. 2.—Above, lateral view of specimen from one of author's cases. Below, normal.

years ago. However, during the past three years and a half, using a careful autopsy technic, I have observed 51 cases of occipital osteodiastasis in autopsies performed by me in three different hospitals.

This report is a clinical correlation and report of incidence of 32 consecutive cases of the injury noted in the autopsies performed by me at the New York Lying-In Hospital during a period of two years start-

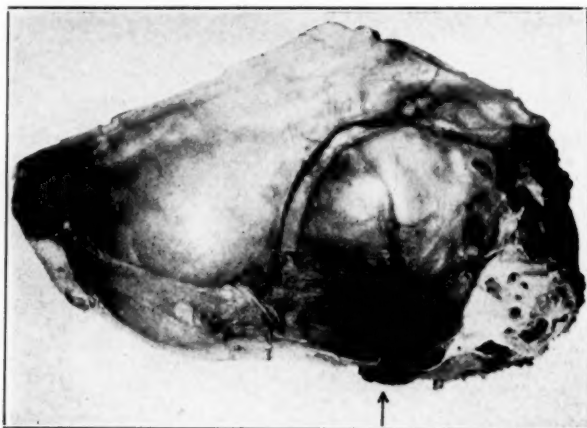


Fig. 3.—Internal surface of occipital bone with a portion of bone removed to show a cross-section of the injury. Unretouched photograph.

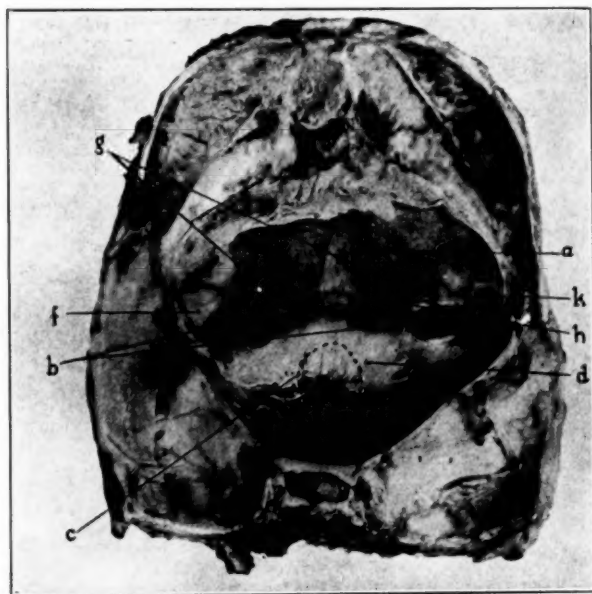


Fig. 4.—Specimen from a case of primary breech extraction. *a*, squama occipitalis; *b*, para lateralis; *c*, position of foramen magnum; *d*, reflected dura; *f*, temporal fontanel; *g*, separation of bones at the posterior intraoccipital synchondrosis; *h*, avulsion of insertion of posterior atlantooccipital ligament; *k*, fracture of fragment adjacent to the temporal fontanel. Unretouched photograph.

ing Nov. 1, 1929. The skull was opened by the method of Beneke,⁴ using a pair of heavy scissors to cut the bone flaps.

The Wassermann test on the mother was positive in two cases and negative in the others. The presentations are listed in Table I. Table II shows the types of delivery of the 22 cases. The 2 cases of spontaneous vertex delivery were cases in which considerable difficulty was experienced in extracting the shoulders. Both occurred on the Out-Door Department. Of the 10 forceps deliveries only one was a low forceps. None of the version and extractions were of the so-called elective type. The stillbirths and deaths are enumerated in Table III. Table IV shows that the degree of occipital injury varied from unilateral separation without displacement to bilateral separation with overriding and gross cerebellar trauma. Twenty-three cases showed overriding and twelve showed gross cerebellar injury. In two cases other cranial bones were fractured. The significance of occipital osteodiastasis without overriding, which was noted in nine of these cases, is largely a matter of speculation. It would seem, if the separation is caused by a compressive force, that

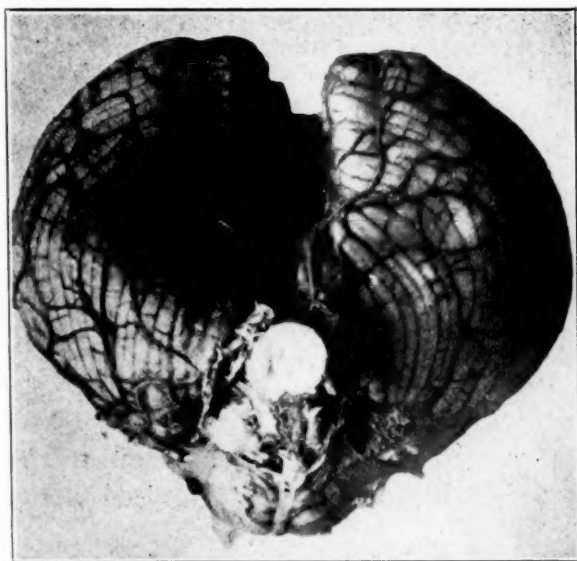


Fig. 5.—Inferior surface of cerebellum showing the depression caused by the displaced inferior portion of the squama occipitalis. Unretouched photograph.

internal displacement and cerebellar compression must occur from the time that the bones are separated until the causative force is removed and the bones return to their normal position.

Table V shows, in the last column, the incidence of occipital osteodiastasis in the various types of delivery. One hundred and sixty-six autopsies were performed among 232 viable fresh stillbirths and neonatal deaths, an autopsy rate of 71 per cent. The occipital injury was found in 19 per cent of the autopsies. This table shows also a figure of 2.8 per cent for the corrected stillbirth and neonatal death rate (to the tenth day) on the 8430 deliveries covered by this study. The 48 autopsies performed on cases delivered by breech extraction after version and primary breech extraction are considered further in Table VI. This table shows the relative incidence of the 20 cases of occipital injury in these groups to other important cerebral and spinal injuries. The totals show that in these types of delivery the incidence of occipital osteodiastasis was equal to that of subdural cerebral hemorrhage and laceration of the falx or tentorium and almost double that of

fracture of vertebra. The majority of the vertebral fractures seen by me were actually epiphyseal separations, the term being used in its general sense.

TABLE I. PRESENTATIONS

Vertex	22
Occiput anterior	12
Occiput posterior	5
Occiput transverse	5
Face	1
Shoulder	2
Breech	7

TABLE II. TYPES OF DELIVERY

Spontaneous vertex with extraction of shoulders	2
Forceps delivery of vertex presentations	10
Low	1
Mid	5*
High	4
Primary breech extraction without forceps	5
Primary breech extraction with forceps on the after-coming head	2
Version and breech extraction	13

*Including one case delivered by Latzko cesarean section after three attempted mid A forceps.

TABLE III. THIRTY-TWO INFANTS

Stillbirths	15
Neonatal deaths	17
Lived less than one hour	11
Maximum age of any case, four days	

TABLE IV. PATHOLOGIC DETAILS OF THIRTY-TWO CASES OF OCCIPITAL OSTEODIASTASIS

Unilateral diastasis	7
Overriding	3
Gross cerebellar trauma	1
Bilateral diastasis	25
Overriding	20
Gross cerebellar trauma	11

Survey of the histories and autopsy findings of the 32 cases shows that the occipital injury constituted an adequate anatomical cause of death in 50 per cent of the cases. In the other cases the occipital injury was associated with other serious lesions, such as fracture of vertebra, and in some cases it was of a minor degree. In some of the stillbirths the fetus was probably dead before the injury occurred, but in none of the cases had the life of the fetus been despaired of.

TABLE V. OCCIPITAL OSTEODIASTASIS IN VARIOUS TYPES OF DELIVERY WITH INFANT MORTALITY AND AUTOPSY RATE*

NEW YORK LYING-IN HOSPITAL, NOV., 1929 TO NOV., 1931

TYPE OF DELIVERY	NO.	STILLBIRTHS AND NEONATAL DEATHS		AUTOPSIES		OCCIPITAL OSTEODIASTASIS	
		NO.	PER CENT	NO.	PER CENT	NO.	PER CENT OF AUTOPSY CASES
Breech extraction after version	117	35	30	27	77	13	48
Primary breech extraction	227	28	12	21	75	7	33
Forceps	858	51	6	30	59	10	33
Spontaneous	7228	118	1.6	88	75	2	2.3
Totals	8430	232	2.8	166	71	32	19

*The following cases are omitted from the figures: 95 macerated fetuses, 46 congenital deformities incompatible with life, 197 premature fetuses (1000 to 1500 gm.), 59 abortions, and 8 craniotomies.

TABLE VI. OCCURRENCE OF CERTAIN CEREBRAL AND SPINAL INJURIES IN FORTY-EIGHT AUTOPSIES OF VIABLE NEONATAL DEATHS AND STILLBIRTHS FOLLOWING BREECH EXTRACTION AFTER VERSION AND PRIMARY BREECH EXTRACTION

NEW YORK LYING-IN HOSPITAL, NOV., 1929 TO NOV., 1931

														TOTALS
Number of autopsies	4	3	5	1	1	1	5	1	1	2	7	3	14	48
Occipital osteodiasis	4	3	5	1	1	1	5							20
Fracture of vertebra			5	1	1			1	1	2				11
Laceration of falx or tentorium		3		1	1		5			2	7			19
Subdural cerebral hemorrhage					1	1	5		1	2	7	3		20

MECHANISM OF THE INJURY

On the after-coming head the injury is apparently produced by impingement of the subocciput against the symphysis pubis. In forceps deliveries the injury is produced by traction in the wrong direction forcing the subocciput against the symphysis. This probably occurs before the head reaches the perineum otherwise we should find a high percentage of these injuries in low forceps cases, which constituted the majority of all forceps deliveries, whereas among 10 forceps cases showing occipital osteodiasis only one was a low forceps. Dysproportion is a contributory cause. Among the 32 cases were 12 cases of contracted pelvis and seven other cases in which the fetus weighed 4200 gm. (9 pounds 3 ounces) or more. Improper forceps application over the occipital bone may tear the squama from the lateral portions. A case is reported in the literature, and I have seen one case (not included in this series), in which the separation resulted from powerful uterine contractions in the presence of dysproportion. The history of several cases suggests that manual traction applied to the occiput and chin to effect the delivery of impacted shoulders may have caused, or increased the degree of, occipital osteodiasis.

CLINICAL DIAGNOSIS

Clinically the diagnosis of this injury cannot be made by external palpation because of the thickness of the soft parts overlying the synchondrosis. Lateral view roentgenogram should demonstrate the injury in cases with marked displacement.

HISTORICAL

Schroeder³ in 1871 described this injury in terms indicating that he had seen a number of cases but he gave no case histories. He said, in part, "In the great number of cases the separation is associated with hemorrhage into the cranial cavity, which, because of the proximity of the medulla oblongata, proves fatal." Winter's⁵ case, reported in 1887, was an easy extraction of a breech presentation. The child was asphyxiated and efforts at resuscitation were unsuccessful. At autopsy the occipital squama was found completely torn from the lateral portions. The only hemorrhage noted was extravasation, especially at the base, between the pia and the brain. Hartman's⁶ case, reported in 1911, was a spontaneous vertex delivery in which the left frontal bone was held at the promontory forcing the occiput under the symphysis. Autopsy showed a depressed fracture of the left frontal bone and depression of the right lateral portion beneath the occipital squama. In 1921 Warwick,⁷ in a review of 200 autopsies on the newborn, mentioned one case of dislocation of the occipital bone causing fatal hemorrhage.

DISCUSSION

With only three reports in the literature, recent obstetric textbooks naturally mention fracture of the occipital bone as being of rare occurrence. It seems curious that this injury has not been reported among the 2917 cases included in the careful studies of fetal and neonatal death by Holland,¹ or Cruickshank,⁸ or Palmer,⁹ or Holland and Lane-Claypon.¹⁰ Study of the various publications on the causation of fetal death suggests that attention has been so sharply focused on cerebral hemorrhage and tentorial laceration that the base of the skull has been forgotten. The efforts toward the reduction of obstetric infant mortality must be based upon thoroughly performed autopsies and to overlook the posterior skull fossa and its contents is to miss the Heel of Achilles of the newborn infant.

CASE HISTORIES

It is impracticable to present in detail all of the 32 case histories. The following histories, selected from those in which the occipital injury was the probable cause of death, are illustrative of the various types of delivery.

CASE 2.—(No. 80429.) Mother was a white primipara, aged forty. Pelvis was normal. Presentation was right occiput posterior which rotated spontaneously to anterior. First stage of labor lasted eight and one-half hours, second stage four and one-half hours. One-fourth grain of morphine was given. Delivery was by low forceps. During forty minutes 8 ounces of ether inhalation was given. Cord was coiled once about the neck. After several minutes' delay the child gasped several

times and did not respond to stimulation of warm bath or adrenalin min. iii into the heart. Heart action ceased after ten minutes. The child weighed 3100 gm. Autopsy, anatomical diagnoses: occipital osteodiastasis with internal displacement and overriding of the inferior squamous border; indentation of the inferior cerebellar surface; partial atelectasis.

CASE 7.—(No. 81226.) Mother was a white para v, aged twenty-four. Pelvis was flat. Presentation vertex, left occiput anterior. First stage of labor lasted twenty-seven hours, second stage twenty minutes. Two rectal instillations of ether were given. Because of nonengagement of head, partial prolapse of cord, and fetal distress, the cervix was manually dilated and the child delivered by internal podalic version and breech extraction. The child's respirations, which were initiated by rubbing the back, were only superficial and it died after five hours. It weighed 5100 gm. (11 pounds 3½ ounces). Autopsy, anatomical diagnoses: occipital osteodiastasis with internal displacement and overriding of the inferior squamous border; indentation of the inferior cerebellar surface; aspiration of amniotic fluid.

CASE 16.—(No. 83318.) Mother was a white primipara, aged twenty-nine. Pelvis was normal. Presentation was vertex, right occiput transverse which rotated spontaneously to anterior. First stage of labor lasted fifty-eight hours, second stage seven hours. Delivery was by mid B forceps. Operative indication was arrest in midpelvis. Right mediolateral episiotomy. Difficulty was experienced in delivery of the shoulders. Fetal heart sounds were not heard during the last half hour before delivery. The child was stillborn and weighed 4200 gm. Autopsy, anatomical diagnoses: excessive molding, elevation of parietal bones and depression of superior border of occipital bone resulting in depression of left occipital lobe of cerebrum; separation of occipital squama from the left lateral portion with moderate internal displacement of the left inferior squamous border.

CASE 20.—(No. 92606, Out-Door Department.) Mother was a white para ix, aged thirty-nine. Pelvis was normal. Presentation was vertex, left occiput anterior. First stage of labor lasted three hours, second stage forty-five minutes. Fetal heart was not heard in second stage. There was a spontaneous delivery of head. Shoulders were impacted for twenty minutes. The child was stillborn and weighed 4250 gm. It had not passed meconium. Autopsy, anatomical diagnoses: atelectasis; numerous subserous petechiae of thoracic organs; small subcapsular hematoma of liver; occipital osteodiastasis with internal displacement and overriding of inferior squamous border; indentation of the inferior cerebellar surface.

CASE 21.—(No. 84419.) Mother was a white gravida ii, para i, aged nineteen. Pelvis was flat with high promontory. Presentation vertex, left occiput anterior. First stage of labor lasted forty-one hours, second stage seven and three-fourths hours. One-fourth grain of morphine was given. Delivery was by high forceps. The child did not breathe and the heart ceased beating after thirty minutes. It weighed 3500 gm. Autopsy, anatomical diagnoses: bilateral laceration of tentorium, right complete, left incomplete; flattening of cerebellum from above; occipital osteodiastasis with internal displacement and overriding of the inferior squamous border; cerebral hemorrhage, slight subdural supra- and infratentorial.

CASE 29.—(No. 85498.) Mother was a white Puerto Rican primipara, aged twenty. Pelvis was generally contracted. Presentation vertex, left occiput anterior. First stage of labor lasted about ninety-six hours, second stage one hour. One-fourth grain of morphine was given. Operative delivery was done because of maternal exhaustion. Internal podalic version and breech extraction was accomplished after manual dilatation of cervix. The child took only one breath and the heart action

ceased after ten minutes. The child weighed 3300 gm. Autopsy, anatomical diagnoses: occipital osteodiastasis with internal displacement and overriding of inferior squamous border; depression of the inferior cerebellar surface; small lacerations of falx and tentorium without hemorrhage; a few subserous petechiae of heart and lungs; aspiration of amniotic fluid.

CASE 30.—(No. 86031.) Mother was a white primipara, aged twenty-one. Pelvic outlet was slightly contracted. Presentation breech, double footling. First stage of labor lasted seven hours, second stage fifty minutes. Delivery was by extraction. Right mediolateral episiotomy was done. Piper forceps were used on after-coming head. Child did not breathe spontaneously and the heart ceased beating after forty-five minutes. The child weighed 3625 gm. Autopsy, anatomical diagnoses: atelectasis; moderate intraventricular and slight subdural cerebral hemorrhage; bilateral complete laceration of tentorium; occipital osteodiastasis with internal displacement and overriding of the inferior squamous border.

CASE 32.—(No. 86236.) Mother was a colored primipara, aged thirty-five. Funnel pelvis with contraction of outlet. Presentation was a vertex, right occiput posterior. Analgesia, complete Gwathmy technic. Delivery was by mid A forceps because of arrest in midpelvis. Head was brought to the perineum and then rotated with forceps to anterior position. Shoulders were delivered with difficulty. The child gasped only twice and heart action ceased after twenty minutes. The child weighed 3900 gm. Autopsy, anatomical diagnoses: atelectasis; occipital osteodiastasis with internal displacement and overriding of the inferior squamous border; indentation of the inferior cerebellar surface; bilateral incomplete laceration of tentorium; moderate subdural supra- and infratentorial hemorrhage; simple fracture of left clavicle; congenital anomaly, accessory digit of both hands.

SUMMARY AND CONCLUSIONS

The synchondrosis between the pars squama and pars lateralis of the occipital bone, because of its weakness and close proximity to the medulla oblongata, makes the base of the fetal skull susceptible of grave traumatic injury during delivery. This injury consists of a separation which may conveniently be called an osteodiastasis since the term fracture is inapplicable. Although this injury was first described by Schroeder in 1871 only three cases are described in the literature. From a series of 51 cases of occipital osteodiastasis seen by me I present a clinical correlation and study of incidence of 32 cases occurring in 166 consecutive autopsies performed by me on viable fresh stillbirths and neonatal deaths during a period of two years at the New York Lying-In Hospital. The autopsy rate was 71 per cent. Occipital osteodiastasis was found in 48 per cent of the autopsies on patients delivered by version and breech extraction; in 33 per cent each of the autopsies on cases of forceps delivery and of primary breech extraction; and in 2.3 per cent of autopsies on cases of spontaneous delivery. Seventy-two per cent of the injuries showed the squama depressed beneath, and overriding, the pars lateralis, and 38 per cent showed gross traumatic injury of the cerebellum. In 48 consecutive autopsies on cases delivered by version and extraction and by primary breech extraction, occipital osteodiastasis occurred in 42

per cent of the autopsies, a frequency equal to that of subdural cerebral hemorrhage and of tentorial laceration and twice that of fracture of vertebra. In forceps deliveries this occipital injury was found in one-third of the thirty cases examined postmortem. Its occurrence in low forceps delivery was rare. The injury was found twice in spontaneous vertex deliveries when extreme difficulty was encountered in the delivery of the shoulders.

My analysis of the mechanism of occipital osteodiasis suggests the following points for its prevention:

1. In forceps deliveries careful cephalic application should be made and the line of traction should not force the occiput directly against the symphysis.
2. In delivery of the after-coming head the occiput should be protected at the symphysis by attention to the direction and force of traction.
3. Manual traction on the head for the delivery of shoulders should be applied to the sides of the head, avoiding the occiput.

Thanks is due Dr. James A. Harrar, Chief Surgeon of the New York Lying-In Hospital at the time this study was made, for his criticisms and permission to report these cases, and to Professor J. P. McMurrich for his suggestions on nomenclature.

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161 WEST SIXTY-FIRST STREET

BACTERIOLOGIC FINDINGS IN THE UTERUS DURING LABOR AND THE EARLY PUERPERIUM*

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THE bacteriologic findings in the uterus during labor and the puerperium have been the subject of intensive investigations. The results, in general, may be said to be quite diverse and in many instances contradictory. The work of Schwarz and Dieckman,¹ Harris and Brown,² Schottmüller,³ Colebrook,⁴ and many other investigators

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has tended to solve the difficult problem. Many of the investigations have dealt only with patients who had severe types of puerperal infection. Other investigators have attempted to study the bacteriologic findings in the uterus during milder and often low grade types of infection. The comparison of studies on such widely divergent groups is sometimes very misleading.

The present investigation is a summary of the routine work that has been carried out in the Woman's Clinic of the New York Hospital from Sept. 1, 1932, to April 8, 1933. The lochia examined were obtained from 171 consecutive uterine cultures, taken during the puerperium, a few on the day of delivery, and a few as late as the seventh day postpartum. The average time of taking the cultures was 3.2 days postpartum. Patients admitted to the hospital postpartum are excluded, and only patients having had full-term and premature deliveries in the hospital are presented in this study.

All patients having a rise in temperature to 38° C. (100.4° F.) in any two twenty-four-hour periods, not including the first twenty-four hours after delivery, are routinely cultured, unless there is some definite contraindication, such as a very deep laceration of the cervix which had been repaired following delivery. In addition to these, cultures were obtained from many patients who had only one temperature rise to 38° C., as well as from a number whose temperatures never exceeded 37.8° C. In the latter group we included patients who repeatedly had daily elevations of temperature not exceeding 37.8° C., the temperature course suggesting a low grade type of infection. In other instances some cultures were taken from patients who were practically afebrile.

A further series of 20 patients on whom cesarean section was performed had cultures taken at the time of operation. When possible, these cultures were obtained both intraovularly and extraovularly.

THE TECHNIC OF TAKING INTRAUTERINE CULTURES

The procedure is always carried out in bed, the patient lying on her back. The preliminary preparation of the patient consists of the usual "perineal care" as carried out by a nurse, consisting of down strokes over the vulvar area with absorbent cotton soaked in green soap, sterile water, and oxycyanide in turn. The legs are then flexed and abducted, while a sterile douche pan is placed under the buttocks. The perineum is now prepared with Scott's solution of alcohol-acetone-mercurochrome. Three sterile towels are used to drape the field. The labia are separated and a bivalve speculum is gently inserted. With the blades of the speculum in the anterior and posterior fornix, the lips of the cervix are everted. In the event of an excess of lochia, this may be swabbed out with sterile sponges. With adequate lighting, a modified Little's tube is inserted, touching nothing prior to its entrance into the cervical canal. Suction is then exerted and generally no difficulty is encountered in completely filling the tube with lochia.

The laboratory technic can be briefly described as follows: The culture tube, containing the lochia, is wrapped in two sterile towels and immediately taken to the

bacteriology laboratory in the clinic. Here the tube is filed, flamed, and broken, and a small swab inserted into the lochia from which all inoculations are made. Five per cent rabbit blood agar plates are streaked, one of which is incubated aerobically, and the other anaerobically in an anaerobic jar modified from that described by Brown.⁶ Plain broth and cooked meat media which is sealed under vaseline are then inoculated. At the time of inoculation direct smears are examined. All media is incubated forty-eight hours and then examined, and subcultures are made as desired. No human serum or ascitic fluid is added to the media, which would facilitate the growth of the gonococcus, and this might explain the absence of this organism in the findings reported.

We have studied the lochia from 171 consecutive uterine cultures obtained during the puerperium. These patients are divided into four groups.

Group 1 consists of 37 patients, some of whom were practically afebrile and in none of whom a temperature exceeding 37.8° C. was recorded, temperature readings being made every four hours, excepting when patients are asleep, throughout their entire stay in the hospital. Both spontaneous and operative deliveries are included in this group.

Group 2 comprises 47 patients who had spontaneous deliveries with no vaginal or intrauterine manipulations, such as cervical repair or repair of laceration of the perineum. In this group the temperature reached at least 38° C. on one or more occasions, not including the first twenty-four hours postpartum.

Group 3 constitutes 42 patients who had spontaneous deliveries and repair of the vagina, perineum, or cervix, and who had febrile puerperia, the temperature reaching at least 38° C. on one or more occasions not including the first twenty-four hours postpartum.

Group 4 consists of 45 patients who had operative deliveries with or without repair, and who had febrile puerperia to the extent that the temperature reached at least 38° C. on one or more occasions after the first twenty-four hours postpartum.

ANALYSIS OF THE FINDINGS IN THE FOUR GROUPS

Percentages as appearing in Charts 1 to 6 are calculated from the incidence of each specific organism in each group isolated, as compared to the total number of patients cultured. With the isolation and identification of species we do not imply that the findings are necessarily a single strain. An analysis of the *composite* findings of all four groups (Chart 1) shows that 65.5 per cent of the organisms recovered are anaerobic streptococci. An additional 8.1 per cent were classed as anaerobic streptococci, but facultative aerobes, so that the combined incidence of anaerobic streptococci, including the facultative group, is 73.6 per cent. Repeated cultivation of these strains was not always carried out unless it was necessary for identification. Accordingly, some strains classed as anaerobic streptococci are not necessarily obligatory anaerobes. The percentage incidence of other organisms found in all four groups are as follows:

26.8 per cent anaerobic diphtheroids
23.3 per cent anaerobic staphylococci
6.4 per cent anaerobic gram-negative bacilli
3.5 per cent anaerobic gas bacilli
13.4 per cent aerobic nonhemolytic streptococci
14.0 per cent aerobic green streptococci
8.7 per cent aerobic diphtheroids
8.7 per cent <i>B. coli</i>
4.6 per cent <i>Staphylococcus albus</i>
0.5 per cent <i>Staphylococcus aureus</i>
0.5 per cent <i>B. proteus</i>
1.1 per cent monilia
8.1 per cent showed no growth

An analysis of this composite group in the four subgroups previously mentioned is possibly more instructive.

In Group 1 (temperature never exceeding 37.8° C.) the incidence of the anaerobic streptococci, including the facultative group, is 64.8 per cent (Chart 2).

Anaerobic staphylococci and anaerobic diphtheroids	24.3 per cent each
Anaerobic gram negative bacilli	8.1 per cent
Anaerobic gas bacilli	5.4 per cent
Aerobic nonhemolytic streptococci	2.7 per cent
Aerobic green streptococci	13.5 per cent
<i>B. coli</i>	5.4 per cent
<i>Staphylococcus albus</i>	2.7 per cent
Monilia	2.7 per cent

In this group 21.6 per cent of the cultures were negative. It should be noted that 2 patients, or 5.4 per cent, had anaerobic gas bacilli in their lochia, both having had operative deliveries. One of these two, an unregistered patient, having had two vaginal examinations before admission to the hospital, had a breech extraction with the application of Piper forceps on the after-coming head. The other, also an unregistered patient, with a transverse presentation, had a version and extraction followed by manual removal of the placenta. Two patients also had colon bacilli in the uterine lochia. One of these had a bougie, followed by a bag, for induction of labor. The second had a spontaneous delivery, with no repair. Urine cultures were not taken on either patient.

In Group 2 (spontaneous delivery without repair, having febrile puerperia) (Chart 3) the incidence of the anaerobic streptococci is slightly higher—being 85.1 per cent, including the facultative anaerobic streptococci. Otherwise, the incidence is practically identical to that in Group 1, with two exceptions; there were no anaerobic gas bacilli isolated, and the percentage of negative cultures dropped to 4.2 per cent.

Two patients had colon bacilli in the uterine culture, one with the diagnosis of pyelitis—although a urine culture was not taken; the other also with a clinical diagnosis of pyelitis and with the colon bacillus in the urine.

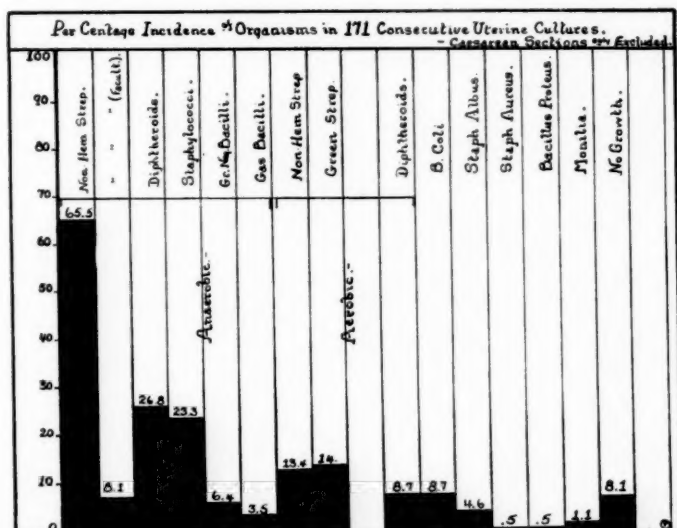


Chart 1.

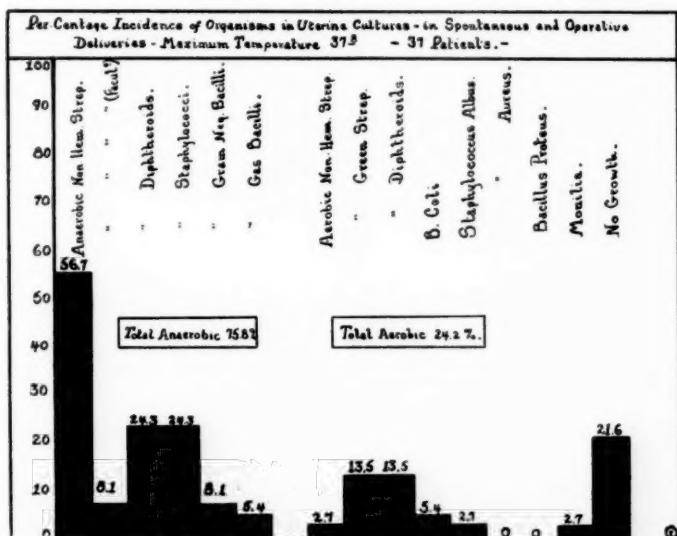


Chart 2.

Group 3 (spontaneous deliveries plus repair) (Chart 4) had a total incidence of anaerobic nonhemolytic streptococci, including the facultative streptococci, of 76 per cent. The incidence of other organisms remains about the same, with the exception of an increase in the number of

aerobic streptococci. Again no anaerobic gas bacilli were recovered. Five patients in this group had *B. coli* in the lochia. The first patient had a clinical diagnosis of cystitis, and *Staphylococcus albus* was found in her urine. The second patient had a clinical diagnosis of

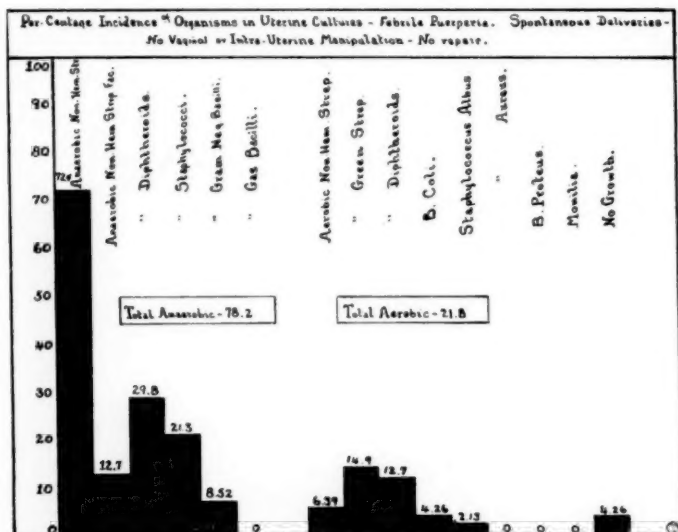


Chart 3.

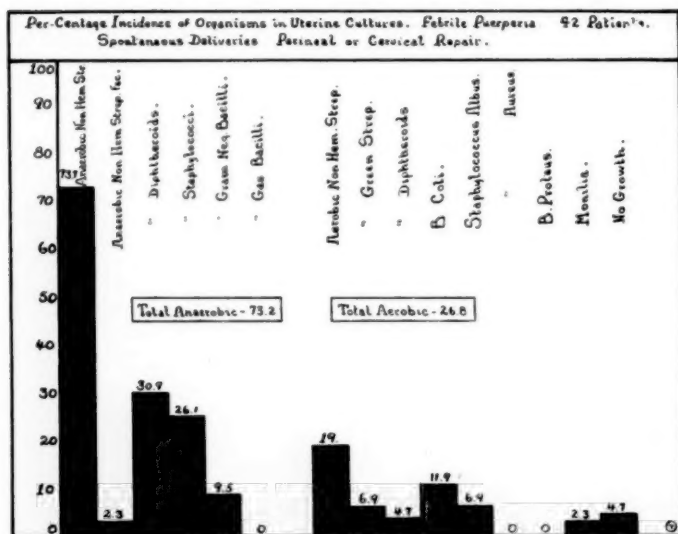


Chart 4.

pyelitis with *B. coli* in the urine. The third patient, delivered of twins, had a perineal and cervical repair. The urine culture was negative. The fourth patient had a clinical diagnosis of pyelitis, and *B. coli* was found in the urine. The fifth patient had a diagnosis of

puerperal infection, and the bacteriologic examination of her urine was negative.

It will be noted that the incidence of the colon bacillus increased to 11.9 per cent in this group, while in the two previous groups it was 5.4 per cent and 4.26 per cent, respectively.

In Group 4 (operative deliveries) (Chart 5) the incidence of anaerobic nonhemolytic streptococci, including facultative aerobes, is 66.5 per cent. The anaerobic staphylococci and anaerobic diphtheroids have essentially the same incidence as in the other groups. *B. coli* was found in 13.3 per cent of the patients, an incidence three times as great as in the spontaneous delivery group with no repair. The first patient had a breech extraction with the application of Piper forceps to the after-

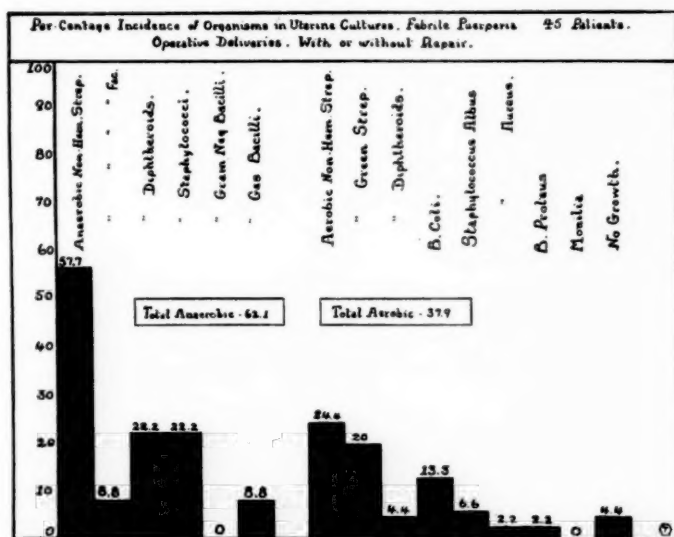


Chart 5.

coming head. The second had an acute inversion of the uterus, which was replaced from below and the uterus packed. In both these patients the colon bacillus was not found in the urine. The third patient had a low forceps and *B. coli* was recovered in the urine. The fourth patient had a breech extraction with forceps application to the after-coming head, and the urine culture was negative. The fifth patient had a low forceps application and was suffering from subacute bacterial endocarditis. *B. coli* was found in her urine. The last patient had a breech extraction, manual removal of the placenta, and repair of the cervix. Urine culture in this instance was not taken.

The incidence of the anaerobic gas bacillus in this group was 8.8 per cent, a total of 4 patients. The first patient had a face presentation with a low forceps. She had a temperature of 38° C. on two days and 39° C. on one day. The second patient had a dilatation of a vaginal

septum and low forceps, with a temperature of 38° C. on two days and 39° C. on one day. The third patient had subacute bacterial endocarditis. The fourth patient had a manual removal of the placenta and repair of the cervix, following breech extraction. She had a temperature up to 38° C. for four days.

In reviewing each species separately (Chart 6), it will be seen that the incidence of anaerobic streptococci was by far the largest in each of the four groups, with an incidence of about 65 per cent in the first and fourth groups, and a slightly higher incidence in the two groups of spontaneous deliveries. As explained previously, these are not necessarily strict anaerobes, but rather a group of obligatory anaerobes and facultative aerobes.

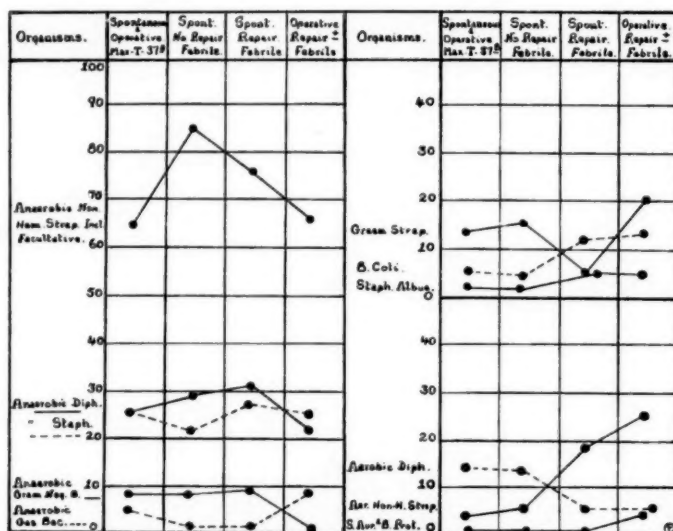


Chart 6.

The frequency of the anaerobic staphylococcus was essentially the same throughout. This was also true of the anaerobic diphtheroids. Anaerobic gas bacilli were recovered in the lochia of a total of 6 patients, 2 of whom had afebrile puerperia, the temperature never reaching 38° C. It will be noted also that these organisms were recovered only in the lochia of patients who had an operative type of delivery.

The organisms included under the heading anaerobic gram-negative bacilli occurred with the same frequency in each of the first three groups, being about 8.5 per cent. These organisms are strict anaerobes. Morphologically, they are slender gram-negative rods, pleomorphic, varying in length from about four to twenty microns, and resembling the *Actinomyces pseudonecrophorus* described by Harris and Brown.⁷ Up to the present time we have been unable to isolate these organisms routinely in pure culture.

Aerobic nonhemolytic streptococci were found nearly five times more frequently in the last two groups than in the first two groups. In other words, in our series this organism is more apt to be found in the uterine culture of patients who have had an operative type of delivery or a spontaneous delivery with a repair.

The incidence of the aerobic green streptococci did not vary greatly in the different groups.

The aerobic diphtheroids were somewhat higher in the first two groups. The incidence of the colon bacillus in the lochia was almost three times as high in the patients who had a repair or operative delivery as in the patients with a spontaneous delivery without repair. In every instance, with two exceptions, where colon bacilli were recovered in the uterine lochia, one of two conditions prevailed: either the patient had a repair or operative delivery, or she showed colon bacilli in her urine.

Staphylococcus albus was recovered in only 8 patients in the entire series. It was found three times more frequently in the group with repair or operative delivery than in the nonoperative group.

B. proteus was found on only one occasion in the entire series. *Staphylococcus aureus* also was found on only one occasion. Both of the latter organisms were recovered in the lochia of patients who had had an operative type of delivery.

Fourteen patients in the entire series had negative cultures from the uterine lochia.

COMPARISON OF URINE AND UTERINE CULTURES

Of the 171 patients, in whom uterine cultures were taken, 121 had bladder urine cultures. Some of these women had clinical signs and symptoms of disease in the urinary tract, while others had none. Of these 121 cultures taken, 50 were negative; while in the remaining 71 positive cultures, there were 22 instances in which organisms were recovered in the urine resembling organisms recovered in the uterine lochia, morphologically and culturally. The colon bacillus was recovered in 6 patients in both lochia and bladder urine. Green streptococci were recovered four times from both sources. The anaerobic streptococcus was found once in each culture. Aerobic diphtheroids were recovered on two occasions from both sources. *Staphylococcus albus* was found four times in both sources. Aerobic nonhemolytic streptococci were recovered seven times from both sources. *B. proteus* was found on one occasion in both cultures.

We may regard these bacteriologic findings in another way, and state that a study of 76 urine cultures in spontaneous deliveries showed similar organisms in urine and uterine lochia ten times, while in 45 patients who had operative deliveries, the bladder urine and lochia had similar organisms in culture on twelve occasions. This

shows quite a marked tendency for an increase in the similarity of the two cultures in the operative group.

COMPARISON OF BLOOD AND UTERINE CULTURES

Thirty-five of the patients in our series had 47 blood cultures. Of these patients, 17.11 per cent showed positive blood cultures. Two-thirds of the positive blood cultures were from patients in the operative group. The other one-third was from patients who had spontaneous deliveries with no repair. No attempt was made to prove the similarity of identity from a serologic point of view of the organisms recovered from the blood stream and uterine lochia. On two occasions the organisms were morphologically and culturally the same.

Aerobic diphtheroids were found in the blood stream of one patient who had aerobic nonhemolytic streptococci in the uterus. In another instance, aerobic diphtheroids were recovered from the blood stream when only anaerobic organisms were present in the uterine lochia. Anaerobic diphtheroids were recovered in the blood stream of another patient who had anaerobic streptococci in the uterine culture. The work of Mellon⁸ and others suggests a very close relationship between the diphtheroids and streptococci. Green streptococci were recovered in the blood stream of 1 patient who had subacute bacterial endocarditis, and the organism was not recovered in the uterine lochia four days postpartum, although a similar organism was present in the urine.

RESULTS OF UTERINE CULTURES AT THE TIME OF CESAREAN SECTION

Twenty additional patients, on whom cesarean section was performed, were studied, the cultures being taken at operation. Whenever possible, both intraovular and extraovular cultures were taken.

Thirteen of the 20 patients had negative cultures. Of these, 7 had elective cesarean sections performed before the onset of labor, and 6 patients had been in labor prior to operation, varying from two to eighteen hours, with an average of 7.6 hours. In each of these 13 patients the membranes were intact at the time of operation, their temperatures reaching 38+° C. on a total of twelve days, but in no instance did any reach 39° C.

Seven of the patients had positive uterine cultures at the time of operation. One of these had an elective cesarean section, and the remaining 6 had been in labor from four to seventy hours, with an average of 27.9 hours. Four patients in this group had ruptured membranes for an average period of 28.8 hours before operation. The temperature reached 38+ C. on a total of sixty-three days, 39° C. on twelve days, and 40° C. on one day. The organisms recovered from the uterine cultures consisted of anaerobic streptococci on three occasions; anaerobic diphtheroids on two occasions; anaerobic gram-nega-

tive rods on two occasions; and anaerobic staphylococci, aerobic non-hemolytic streptococci, *Staphylococcus aureus*, and *B. coli* each on one occasion. *B. welchii* was found once, and that case has been fully reported.

SUMMARY

The bacteriologic findings in the uterine lochia in 171 consecutive uterine cultures is described. The patients were divided into four groups:

Group 1: 37 patients who had afebrile puerperia or had low grade fevers, the temperature never exceeding 37.8° C.

Group 2: 47 patients with spontaneous deliveries and no repair.

Group 3: 42 patients with spontaneous deliveries who also had a perineal repair.

Group 4: 45 patients who had operative deliveries with or without repair.

In each of the last three groups the temperature reached 38° C. on one or more occasions, not including the first twenty-four hours post-partum.

In each of the four groups it was noted that anaerobic streptococci were the most frequent organisms found. Anaerobic gas bacilli were recovered only in patients who had operative deliveries. The colon bacillus was found in the uterine lochia more frequently in patients with operative deliveries than in those with spontaneous deliveries. In the latter instance it is often associated with the same finding in the bladder urine. *Staphylococcus aureus* was recovered in only one uterine culture in the entire series. *Staphylococcus albus* was recovered eight times. A group of organisms is classified as anaerobic, gram-negative bacilli. They vary considerably morphologically but were not isolated in pure culture. They grew better in liquid media, and were very difficult to grow anaerobically on the surface of rabbit blood agar. No growth was obtained under aerobic conditions. Some members of this group resemble morphologically the *Actinomyces pseudonecrophorus* described by Harris and Brown.⁷

CONCLUSIONS

1. In 171 consecutive uterine cultures taken during the puerperium, averaging 3.2 days following delivery, the organisms found most frequently were anaerobic streptococci. These organisms, together with the facultative aerobic streptococci, were present in 73.6 per cent of all patients studied.

2. The examination of the cultures revealed the presence of anaerobic gas bacilli in the puerperal uterus following operative deliveries in six instances, an incidence of 3.5 per cent. In one other patient this organism was found to be present in the uterus during labor.

3. The incidence of the colon bacillus in the uterine cultures was 8.7 per cent. This bacillus was found in the uterus almost three times more frequently in operative than in spontaneous deliveries.

4. In the nonoperative patients, in whom the colon bacillus was found in the uterus, there was almost always an accompanying colon bacillus infection in the urinary tract.

5. *Staphylococcus aureus* was found to be present in only one postpartum uterine culture, an incidence of 0.5 per cent.

6. In 6.4 per cent of the uterine cultures we found anaerobic gram-negative bacilli.

7. All patients on whom cesarean section was performed and who showed positive uterine cultures at the time of operation, later developed febrile puerperia.

8. In no instance in the 191 uterine cultures studied was the aerobic *Beta hemolytic streptococcus* found.

9. During the period in which these bacteriologic studies were conducted there were 1,550 full-term and premature deliveries on our service, with no maternal death from infection.

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A SURGICAL CONSIDERATION OF APPENDICITIS IN PREGNANCY*

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THE late John B. Murphy never held his peace when any variety of appendiceal disease was being talked about. He had much to say at many times and in many places of what he termed the "antemortem" surgeon and the "*expectans mortem*" school of surgery, for on the solid rock of immediate operation in acute appendicitis he took his stand, and never in the course of his long and active professional life did he waver in the smallest degree from that position. He was just as positive in his convictions about appendicitis in pregnancy as about appendicitis at any other time. In 1912, in discussing a paper by Palmer Findley on

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this subject, then a rather uncharted territory, he made the unqualified statement that there is never an excuse for delaying surgery in this condition, on the ground that if there is one thing the man of experience has concluded, it is that "he does not know what is going to happen in the ten or the twenty or the forty hours following the onset of appendicitis."

As a surgeon I follow in his train. I have seen too many tragedies, I have personally participated in too many, not to have a very healthy and wholesome fear of what an hour, let alone twelve hours, may bring to pass when one is dealing with this most treacherous of all diseases, and I cannot see that its association with pregnancy alters the situation in any degree. Appendicitis is still appendicitis, and the first indication in it, as the late W. W. Keen said many years ago, is still to call a surgeon, for it is absolutely impossible in any case for any medical man, however gifted he may be, to foretell whether the acute process will subside promptly or whether it will progress to the stage when no treatment is of avail.

I grant, of course, that the surgeon and the obstetrician have somewhat different points of view. They are likely to continue to have them, for that matter, as long as we follow the present insane system of educating the medical youth of the land to believe that each medical specialty is self-limited and self-sufficient. I see with a surgical eye, the obstetrician, not unreasonably, focuses his gaze on the obstetric problem, but I say again that appendicitis is still appendicitis, and I contend that the pregnant woman runs enough risks in the performance of her supposedly physiologic function, without subjecting her to the additional risks of a purely surgical disease that is amenable to cure in the overwhelming majority of cases only when it is surgically treated. The hesitancy of the obstetrician—I would remind you that I am speaking categorically—is natural. His ideal is to save two lives, and he fears that surgery will jeopardize the life of the unborn child. That reasoning, as I shall point out later, is fallacious, and Moynihan's rule is the more logical one, that it is unreasonable to permit an individual to die of one disease simply because he happens to be afflicted with another. The pregnant woman surely has as much right to her chance of life as her nonpregnant sister.

Since appendicitis as a clinical entity is really a modern discovery, it is not surprising to find that until quite recently its association with pregnancy was regarded as something of a surgical curiosity. In 1905, even though the disease had then been recognized for some years, Kelly wrote that the reported cases of appendicitis in pregnancy were still too few to warrant general conclusions. As he points out, the ruptured cecum in a pregnant woman reported by Stumpf in 1836 was undoubtedly an instance of perforated appendicitis, as was the perityphilitic

abscess operated on by Hancock and reported in the *Lancet* for 1848, but relatively little had been written on the subject since appendicitis, as the modern physician knows it, had been fully studied. Within the last decade, however, innumerable studies have been published, chiefly in the foreign literature, and many of the more recent ones, those of Heineck, Jerlov, and Schmid, for instance, run into the hundreds of cases. There is no longer any excuse for reporting the single case, unless, as does not usually happen, it is truly unique, and there is not much excuse for reporting small series of cases. The group of 50 cases which we have investigated for this paper from the records of Charity Hospital, we have studied merely from the clinical side, and not with any idea of making a statistical report.

Since appendicitis is preeminently a disease of the childbearing years, and since gestation confers no immunity to it, it is not surprising that the pregnant woman should exhibit it with more or less frequency, and Kelly is undoubtedly correct in his statement that the association of the two conditions is usually purely accidental. In practically all the reported series the highest incidence is between the ages of twenty and thirty. In our own series the age limits were sixteen and forty-three years; 40 of the 50 patients were under thirty years of age, and 15 were between sixteen and twenty years. The exact incidence is not a matter of moment; in the reported cases it varies from a fraction of 1 per cent, as in the report of Baer, Reis and Arens from the Michael Reese Hospital, to 2.5 per cent, as in the series reported by von Eiselsberg, by Schmid, and by Paddock. The important consideration is that the disease can occur as a complication of pregnancy, rather than how often it develops.

It is beyond question that the woman who has once had appendicitis, the so-called chronic or recurrent disease, is very likely to develop it again during her pregnancy, often with very much graver results. In our own series 31 patients, well over half, gave a story of previous attacks, and that percentage holds for practically all the reported series. The explanation is simple. It has long been recognized that recurrent appendicitis is unfavorably influenced by menstruation, and LeGendre's case, cited by Kelly, in which the menstrual cycle continued to exert its effect on the appendiceal disease even during gestation, when the menses were suppressed, is strong additional proof of that influence. Since this is so, it is perfectly reasonable to assume that pregnancy, which introduces altered abdominal relations and altered constitutional states, should have an even more exciting effect upon latent disease, while the constipation which is usual during pregnancy and the engorgement of the pelvic and hemorrhoidal veins which is physiologic also play their part.

That the appendix shares in the altered relations induced by pregnancy there can be no possible doubt. The radiologic studies of Baer, Reis

and Arens, for instance, upon 78 patients, show definitely that it undergoes a progressive displacement upward after the third month and that it reaches the level of the iliac crest at the end of the sixth month; since it also undergoes a counterclockwise rotation, it is obvious that anatomic and physiologic rest are alike impossible. The situation is even more aggravated, as Kelly points out, if as the result of previous inflammatory attacks the appendix has become adherent to some one of the pelvic structures. Finally, the violent alterations which occur during labor and immediately after delivery necessarily have a deleterious effect on preexisting disease. The recurrence of previous appendicitis in pregnancy is so well established that some writers have gone so far as to suggest the propriety of a prophylactic appendectomy upon all married women in the childbearing years. We should hesitate to countenance so extreme a proposal, but it does seem the part of wisdom to perform an interval operation without undue delay in those cases in which there have been definite recurrent attacks.

Parity seems to play no special part, and the fact that in Heineck's series more than half of the patients were secundiparas seems merely accidental. In our series 19 women were primiparas, and one patient had had 14 previous full-term deliveries. The stage of gestation, however, is more important, the disease becoming increasingly infrequent and increasingly severe as pregnancy advances. The majority of cases occur within the first six months, and, more particularly, within the second trimester, within which period, as we have already pointed out, the appendix becomes transformed from a pelvic to an abdominal organ. In our own series the limits of gestation were six weeks and seven months; 32 patients were in the first trimester, 16 in the second, and 22 in the third. One patient did not know that she was pregnant; the condition was suspected at operation, and was confirmed later by the Friedman modification of the Asehheim-Zondek test.

The pathology of the appendicitis of pregnancy is probably not inherently more serious than the pathology of appendicitis at other times, but it seems more serious, especially in the later months, because it is so often enhanced and aggravated by delay. The gangrenous and ruptured types, in comparative series studied by Baer, Reis and Arens, were respectively $5\frac{1}{2}$ and $3\frac{1}{2}$ times as frequent in the pregnant as in the nonpregnant state, and McDonald reaches the same conclusion from a study of his own and Jerlov's series as compared with the 1,000 nonpregnant cases reported by Quain.

All the literature bears witness to the fact that if the acute case is not promptly treated, rapid spread of the infection is the rule, and that, especially if the pregnancy is far advanced, rupture is likely to be followed by diffuse, spreading peritonitis, with very little tendency to localization and abscess formation. Any other result could scarcely be

expected. The appendix is located high in the abdomen, there are no loops of intestine to limit the extension, and the pus can spread to the pelvis only along the smooth uterine wall. Moreover, the uterus tends to crowd the protective omentum out of the way, and if, as sometimes happens, the uterine wall forms part of an abscess, the results may be disastrous, for the pendulous, heavy organ changes its position on the slightest change of position by the patient. The movements of the child, as Marbury points out, may have all the effect of a drastic cathartic, violent excursions during labor destroy whatever localization may have occurred, and there is an abrupt and extensive alteration in the intraabdominal relations the moment delivery has occurred. Furthermore, the increased vascularity and lymphatic dilatation which are physiologic during pregnancy predispose to the development of phlebitis and thrombosis, while the lessened resistance of the pregnant woman to infectious and toxemic processes is a factor in the morbidity and mortality which cannot be ignored.

If abortion or labor should occur during or immediately after an acute attack, the risks are tremendously increased, for the raw uterine cavity and the gaping, thrombosed sinuses furnish ideal channels for the spread of microorganisms, so that postabortal or postpartal infection is a very serious possibility. That this sort of extension is quite possible was realized even when Kelly wrote, twenty years ago, for cases had been reported in which *B. coli communis* had been found in pure culture in the organs of the fetus, in the placenta, and in the large uterine veins. The high fetal mortality, which is due partly to prematurity and partly to toxemia, may be discounted, for it is largely inevitable, but the part which abortion plays in the final maternal result must be mentioned, for it seems to be overestimated, or, to speak more accurately, to be wrongly evaluated. The incidence of abortion and premature labor naturally increases in exact ratio to the seriousness of the disease. In our own series there was one abortion at two and one-half months and two premature labors in the third trimester, all of them in patients who were gravely ill, and these findings parallel those of other observers: the patient with recurrent or subacute disease, or the patient who is operated upon promptly in her acute attack, is likely to continue her pregnancy undisturbed, indeed, more likely to do so than the patient in whom operation is deferred. Moreover, the disease itself, the fever and toxemia that go with it, the gastrointestinal disturbances, the reflex peritoneal irritation, and the direct extension of the infection, are, as McDonald correctly points out, the factors responsible for the interruption of the pregnancy, rather than the operative act itself, which is the smallest part of the picture. Furthermore, while the maternal mortality is highest among the patients who abort, abortion is not the event which is primarily responsible for the fatality. Many of these women are

overwhelmed by their sepsis and are actually moribund when the fetus is expelled; in other words, they abort because they are dying; they do not die because they have aborted.

The mortality of appendicitis in pregnancy is difficult to gauge, for the reason that the reported figures, being based largely on acute cases alone, are difficult to evaluate. This sort of calculation, in our opinion, is both inaccurate and misleading; the recurrent and subacute types of disease, which are dealt with promptly, before they progress to the acute stage, must in all justice be considered also, and in this group the mortality is minimal. The nonsurgical treatment of the acute disease produces a mortality of approximately 100 per cent, just as it would in the nonpregnant state. Schmid in 486 cases found a mortality of 36.2 per cent for the acute group, which was reduced to 23.7 per cent by the inclusion in the calculations of the chronic cases which formed approximately 20 per cent of the total number and in which there was but one death. In the 362 cases collected by Marbury, 34, approximately 9 per cent, occurred in the last trimester of pregnancy and the mortality in that group was 26.4 per cent. Other observers, using smaller series, estimate the death rate to be 50 per cent and higher. In our own series there was **but one death**, a patient in the third trimester who had a generalized peritonitis and subsequent phlebitis of the pelvic veins, but it must be remembered that 45 of the 50 patients were operated upon before their trouble became serious. We did not select the cases, we took them as we encountered them in the records, and the 26 surgeons responsible for them are to be congratulated on the wisdom they displayed in so seldom temporizing with a disease that particularly under these circumstances can be fanned into fatal activity by delay.

The chief reason for delayed surgery today is failure to recognize the condition, and prompt diagnosis is not as simple as it sounds. Even in the nonpregnant individual appendicitis is very frequently an atypical disease. In the 239 fatal cases of acute appendiceal disease studied from two New Orleans hospitals a few years ago by C. Jeff Miller, less than half of the patients exhibited even the so-called cardinal triad of symptoms, pain, nausea and vomiting, and localized tenderness. If this be true of the uncomplicated case, it is easy to imagine how the changes and chances of pregnancy, particularly as it advances, are likely to introduce further confusion. In the first trimester, morning sickness and the general malaise of early gestation are fruitful sources of error. Right-sided pain is not infrequent, especially between the fourth and seventh months, when the uterus rises into the abdomen out of the pelvis. Constipation and flatulence are general accompaniments of pregnancy, and abdominal distention is often noted before the increasing size of the uterus could possibly be responsible for it. Localized tenderness may be difficult to elicit because of the size of the uterus, and while theoret-

ically the location of the pain at an increasingly high level as pregnancy advances and the appendix and cecum are pushed higher and higher into the abdomen seems an excellent point of distinction, actually it does little more than introduce the possible diagnosis of upper abdominal disease. The movements of the child after quickening are often responsible for abdominal discomfort that amounts to actual pain, and in this connection we might mention that in one of the cases in our own series the patient complained that her pain was aggravated by fetal movements. Marbury and Jerlov also mention this symptom, although Baer, Reis and Arens did not note it. Bimanual examination is seldom satisfactory except early in pregnancy, for in the late months the adnexa are out of reach of the examining fingers. Frankel's suggestion that the patient be examined while lying on her left side, in which position the heavy uterus is at least partially removed from the field of investigation, is a very practical one, though, as Marbury points out, the attenuation and thinning of the abdominal muscles which are constant in late pregnancy tend to minimize muscle spasm. Finally, symptoms in the late months are likely to be considered evidence of beginning labor, and postpartal symptoms may be considered due to postpartal infection.

The laboratory is not very helpful. I am inclined to question its usefulness even in the nonpregnant state, though I employ it, of course, with ritualistic care, and it is even less useful during pregnancy, when leucocytosis is physiologic. Any white count under 12,000 is not likely to be of much diagnostic value, though the increase in polymorphonuclear cells may be significant in connection with other data. In our own series only 4 patients exhibited a white count over 12,000, the extreme being 18,500 in a patient six months pregnant, with sugar in the urine. The patient who died had a leucocytosis of only 12,500, with a 79 per cent polymorphonuclear count. The sedimentation test was not helpful in any case in this series.

The history of previous attacks is perhaps the most valuable single point in the making of a diagnosis, and where this is lacking, an analysis of the clinical signs and symptoms with more than the usual care is the best advice that can be offered. The safest rule is to eliminate nonsurgical complications and then to operate, even without a definite diagnosis, for here, as elsewhere, Deaver's aphorism is applicable, that a hair-splitting diagnosis seldom gets a patient anywhere except to the grave.

The confusion with ectopic pregnancy or with a twisted fibroid or a twisted ovarian cyst is not of great moment, indeed may be rather fortunate, for early operation is indicated in all these conditions, and the mistake in diagnosis may save a life. The confusion with eclampsia, which is sometimes ushered in by epigastric pain, nausea, and vomiting, is seldom lasting, for the proper investigations promptly clear the field.

The most important disease to be differentiated is pyelitis, which is relatively rather frequent in pregnancy, and which is some six times more frequent on the right side than on the left for the purely anatomic reason that the pregnant uterus normally rotates to the right and so may compress the ureter where it crosses the pelvic brim. Laboratory tests, including cystoscopy, usually settle the diagnosis. Polak points out that the sequence of events in appendicitis and pyelitis is not the same, that in appendicitis the sequence is first pain, later fever, and rarely chills, whereas in pyelitis it is chills, fever and pain, which is all very well if the case runs true to form but not much help if it does not. Murphy suggests striking the kidney region with the clenched fist, remarking that the patient, if she has pyelitis, will promptly arise and smite you, and we agree that the test is conclusive, though its limitations are clear. One must bear in mind that the mere presence of pyelitis does not necessarily eliminate appendicitis, though the coincidence would be unusual, and one must also remember that an operation on the mistaken diagnosis of appendicitis is far better than abstinence from operation on the mistaken diagnosis of pyelitis.

Occasionally, even in the quite modern literature, one runs across the suggestion that watchful waiting is a justifiable policy in appendicitis in pregnancy, but the majority of writers, obstetricians and surgeons alike, now take the point of view that the patient with appendicitis is a surgical problem first and an obstetric problem second, and that, while individualization of cases may be permissible to the man of experience in the nonpregnant state, here it can only spell disaster. Once the diagnosis is made, or strongly suspected, immediate operation should be the rule, and, speaking as a surgeon, I can see no reason for conducting it by any but accepted surgical methods. I should not, for instance, drain a ruptured appendix in a nonpregnant woman through the rectum, without laparotomy, and I see no reason for using that technic in a pregnant woman, or for employing any other procedure which so violates sound surgical principles.

In the early months of pregnancy, operation is seldom difficult or complicated, but the difficulties increase, naturally, the nearer term approaches and the more urgent becomes the obstetric factor. The appendix should be removed whenever it can be safely and expeditiously excised; if frank pus is present, and if the appendix is not readily accessible, drainage alone should be done. Manipulations should be reduced to a minimum, and the gravid uterus should be handled as little as possible; under no circumstances should attempts be made to bring it out of the abdominal wound. The decision as to drainage leaves one on the horns of a dilemma. That drainage should be omitted whenever it can be omitted with safety goes without saying, but it must always be instituted when frank pus is present, and it must be remembered, too,

that the peritoneum is less to be trusted in pregnancy than it is at other times. The drainage tubes must be placed with special care, for the changing conditions within the abdomen during pregnancy, particularly if abortion or labor supervenes, are likely to disturb their position. The solution of the problem must rest on the individual judgment of the surgeon as applied to the individual case; fixed rules are impossible. Kelly, by the way, is quite correct in his insistence that while complete drainage of the pelvis is essential, vaginal drainage is not to be considered.

Both the right rectus and the McBurney incision have their advantages. The former gives a better exposure, though in late pregnancy this is of little advantage, since most of the abdominal cavity is obscured by the uterus, while the necessity of crossing a clean intestinal tract to reach the infected field is distinctly dangerous, and when drainage is necessary, infection of the wound is likely, even if the drain is brought out through a stab incision. The McBurney incision has none of these disadvantages, but it is not adequate if the diagnosis is incorrect and exploration must be done, and it is thoroughly unsatisfactory if the appendix is abnormally located. In late pregnancy the incision should be higher and more lateral than it usually is. The continuation of the gestation will naturally put a heavy tax on the operative scar, and the strain will be enhanced if labor follows operation promptly, but a meticulously careful closure, with an extra number of sutures, will eliminate at least part of this difficulty, and it need scarcely be pointed out that a ventral hernia in a live patient is to be preferred to a well-healed wound in a dead one.

Methods of delivery are the business of the obstetrician, but the surgeon who shares the responsibility of the patient with him has a right to comment on them. Accouchement forcé may be summarily dismissed; it was advised guardedly by Kelly in 1905, and in that day there may have been some excuse for it, but it seems strange to find Cooke and Mason in 1920 rather complacently mentioning it as a possibility if the patient be a multipara and her obstetrician an expert. König's method seems to have nothing at all to commend it, surgical or obstetric; he advises drainage of the appendiceal abscess, then vaginal cesarean section, then inspection of the abdomen and closure of possible breaks in the abscess cavity by fine sutures. Porro section is advised by some authorities if the infection is generalized and labor is imminent, but this precaution seems too radical for any but the exceptional case, and not altogether free from danger. DeLee believes appendectomy combined with low cesarean section a safe procedure if the attack should coincide with labor and if labor has advanced sufficiently far for the lower uterine segment to be retracted upward away from the bladder.

A few other writers advocate the simultaneous performance of appendectomy and cesarean section in the acute case at or near term.

Now I have never personally done a cesarean section, in which respect I am probably unique among surgeons, but I have done my share of surgery, and I know enough of the routes of infection to hesitate long before I subjected any patient of mine to such a risk. Your own Society a few years ago, in an exceedingly valuable statistical report, announced a collective mortality of some 16 per cent for cesarean sections done in this community on supposedly obstetric indications, and I do not care to contemplate how that mortality would be increased by even the occasional performance of cesarean section in the presence of abdominal infection.

Speaking merely as a surgeon, whose obstetric days are far behind him, I would say that the simplest and safest solution of the problem is for the surgeon to take care of the appendiceal disease and for the patient, in the absence of obstetric indications, to be left to manage for herself obstetrically; with the aid of Nature, she will probably do a better job than the obstetrician could do for her. Labor is likely to supervene shortly after operation, but if the abdominal closure has been done carefully, and if parturition is shortened by the various methods known to modern obstetric art, then the end-result is likely to be far more satisfactory than any procedure which involves the termination of pregnancy at the time of the abdominal operation. If the maternal disease is grave, the child's chance of survival is too small to warrant increasing the mother's risk for its sake.

The liberal use of morphine for the first few days postoperative will prevent abortion or labor if it is at all possible to prevent it. Purgatives, laxatives, and even enemas should be withheld, distention being controlled by the rectal tube, and it seems scarcely necessary to add the warning that the use of pituitrin is the surest possible way of precipitating the result one is hoping to avoid. Phaneuf mentions the value of enterostomy in serious cases, which permits control of distention, drainage of the bowel, and direct introduction of glucose, with a high measure of safety and with the least possible inconvenience to the patient.

From the point of view of the surgeon, appendicitis in pregnancy in its milder manifestations is little more serious than it is in the non-pregnant woman, though its potentialities for harm are far greater and the wisdom of delayed operation is therefore more questionable. Appendicitis in its acute manifestations, however, is exceedingly serious, and there is even less justification for temporizing with it than there is in the nonpregnant state. Delay does no good to the child, and it places the mother in increasing jeopardy with each succeeding hour. The indication for prompt operation, once the diagnosis is reasonably certain, is clear and uncontrovertible, and the obstetrician and the surgeon who base their performance upon that premise need make no apology for their results.

SUMMARY

1. Appendicitis is a possible complication of pregnancy, which is particularly likely to recur if there has been a history of previous attacks, and which is increasingly serious as pregnancy advances.
2. The pathology is probably no more serious than in the nonpregnant state, but it is aggravated by delay, and, because of anatomic and physiologic considerations, it may quickly exhibit severe and fatal manifestations in the absence of prompt surgical treatment.
3. Abortion increases the mother's risk, but it occurs because of the disease and not because of the surgery instituted to relieve it.
4. The fetal mortality is inevitably high. The maternal mortality is entirely in proportion to the stage of gestation and the severity of the disease; in the mild variety it is little higher than in the nonpregnant state.
5. Diagnosis late in pregnancy is complicated by the various factors which pregnancy introduces, and is almost entirely a clinical matter. Pyelitis offers the chief difficulty in differential diagnosis.
6. Prompt operation is indicated as soon as the diagnosis is made, or reasonably suspected, and the procedure should be conducted throughout on the basis of sound surgical principles.
7. Delivery should be according to obstetric indications.
8. The proper precautions during the immediate postoperative period may serve to prevent abortion or premature labor.

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CANCER OF THE BODY OF THE UTERUS COMPLICATING PREGNANCY

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CANCER occurs in the uterus more often than in any other organ, yet its presence in the body of the pregnant uterus must be exceedingly rare. Frank, in his textbook *Gynecological and Obstetrical Pathology* (p. 290), states that "pregnancy has never been noted in

*Extensive bibliography.

corporeal cancer." However, Schumann, in 1927, reported a case of cancer of the body of the uterus complicating pregnancy. Recently Tracy has reported a case of carcinoma of the body of the uterus associated with tubal pregnancy.

Since 1927 a careful review of the literature shows no further cases.

In 87 cases of cancer of the body of the uterus reported by Healy, pregnancy was not mentioned as a complication. Four of these were under forty years of age. Twenty-five per cent of his cases were multiparas. Donald and Shaw reported 177 cases of cancer of the body of the uterus. Two of this series occurred before the menopause, and one of these was under forty. Smith and Grinnell, in 1927, reported that four of their series of 101 took place under the age of forty. Thirty-six per cent of their patients were never pregnant. Ninety-five of the patients were past the menopause. Baldwin, continuing the reports of Peterson, collected 145 cases of cancer of the body of the uterus. The youngest patient was twenty-two years of age. Mahle collected 186 cases of cancer of the body of the uterus from the Mayo Clinic. In 1925 Taussig reviewed the literature of uterine body cancers in young people. In none of these cases or the following series was pregnancy mentioned as a complication. Norris and Vogt reported 115 cases, with 15 occurring in patients under forty years of age. Cullen, Williams, DeLee, Anspach, Curtiss, Cragin, Crossen, Hertzler, Polak and Webster make no mention of instances where cancer of the body of the uterus complicated pregnancy.

According to Ewing, "the uterus is still probably the most frequent seat of the disease in women . . . and statistics may be cited to show that the uterus is first in the list of organs affected by primary cancer." Norris found that 15.2 per cent of all cancers of the genital tract were in the fundus of the uterus. Frank placed these figures between 10 per cent and 15 per cent. Peterson thought that the average was a little higher, 18.8 per cent, while Wilson found that his series averaged 11.2 per cent. The New York State Institute for the Study of Malignant Diseases found cancer of the body of the uterus constituted 1.7 per cent of the epithelial neoplasms of the uterus.

In the ten-year period between 1921 and 1931 there occurred in the Gynecological Department of the Albany Hospital 477 cases of cancer of the uterus. There were 183 or 38.4 per cent in the body of the uterus while 294 or 61.6 per cent originated in the cervix. There were only three cases of the former below the age of forty years, or 1.8 per cent; while 19.7 per cent of the cancers of the cervix occurred under that age. Seventy-nine and two-tenths per cent of all cancers of the body of the uterus occurred after fifty years of age, while 50 per cent of the cervical cancers were found in patients under fifty.

The figures in Table I show the age incidence of uterine cancers occurring in the Gynecological Department of the Albany Hospital:

TABLE I. YEARS 1921-1931

	TOTAL	UNDER 30	31-40	41-50	51-60	61-70	OVER 70	PER CENT
Fundus	183	1	2	34	78	49	19	38.4
Cervix	294	4	54	90	80	55	11	61.6

Thus, almost 80 per cent of our cases of cancer of the body of the uterus occurred in women over fifty years of age. Peterson found 73.2 per cent between 55 and 65. Koblanck reported 50 per cent between

50 and 60. In spite of the frequency of cancer of the body of the uterus, only a small percentage occurs in the child-bearing ages, which in a large measure would account for the infrequent association of pregnancy and carcinoma of the body of the uterus.

The ratio of cancer of the body of the uterus to cancer of the cervix is less than 1 to 2 in our series. This is very close to the figures of Norris. Peterson and Baldwin found the ratio about 1 to 5, while Koblanek placed it at 1 to 10. Mahle reported that cancer of the cervix was about 3.5 times as common as cancer of the body. In their 649 cases of cancer of the uterus, Smith and Grinnell placed the ratio at 1 to 4.46. The New York State Institute for the Study of Malignant Diseases found their ratio to be 1 to 5.7.

The treatment of cancer of the body of the uterus, except in poor surgical risks, in the Gynecological Department of the Albany Hospital, consists of panhysterectomy and bilateral salpingo-oophorectomy, according to the technic described by Sampson. This includes ligation of the fimbriated ends of both fallopian tubes before attempting to remove the uterus and ligation of efferent vessels; also clamping across the vaginal vault below the cervix. After clamping across the vagina below the cervix a vaginal douche is given and the vagina is wiped dry with bits of gauze before cutting across the vagina below the clamp and removing the uterus. This procedure is followed for two purposes: to prevent the infection of the field of operation with bacteria and to prevent the possible implantation of cancer in the pelvis. We believe that radium should be used only in advanced cases or in patients who are unable to stand an operation.

In the Gynecological Department of the above-mentioned hospital, patients with uterine bleeding are handled in the following manner: If possible a diagnosis is made or appropriate treatment determined without a preliminary or diagnostic curettage. If a diagnosis cannot be made or a hysterectomy is not clearly indicated from the data at hand, a curettage is done.

Parous women are curetted in the Sim's position and usually without an anesthetic. In nulliparous women nitrous oxide is usually employed as an anesthetic.

If carcinoma of the body of the uterus is suspected, a minimal dilatation of the cervix is done and small specially designed ovum forceps introduced into the uterine cavity. Gently an attempt is made to remove enough tissue for diagnosis. If the tissue in the gross suggests cancer, no further manipulation is done until after a frozen section is made. If cancer is not found, the uterine cavity is thoroughly explored both with curette and ovum forceps. If cancer is diagnosed by frozen sections, the uterus is usually removed that morning. Such patients usually come to the operating room prepared for the major operation should it be indicated. In every instance curettings are fixed

in Zenker's solution, imbedded in paraffin and sections obtained in twenty-four hours. This we believe is of great importance not only to obtain permanent sections but also better to enable us to make an early correct diagnosis, when the amount of the material is small or the results of the microscopic examination of the frozen sections are uncertain. Even if on exposing the cervix a polyp is found or bleeding is seen arising from senile changes of the cervix or vagina, the entire uterine cavity is explored. On several occasions we have found an associated cancer of the body of the uterus in these cases.

In all patients with suspected cancer of the uterine cervix, tissue is obtained with a "punch" for microscopic examination, in order to determine not only whether or not cancer is present but also the type. The latter helps determine the form of treatment we may wish to employ. If the removal of the tissue is associated with undue trauma, the area is cauterized with an electric cautery and in some instances acetone is allowed to run into the vault of the vagina with the patient in the knee chest posture. Frequently the tissue is obtained for biopsy with the patient in the knee chest posture rather than the Sim's.

Radium is frequently employed in patients with hyperplasia of the endometrium, myofibrosis and in cervical cancer, the latter being treated with radium alone or radium followed by hysterectomy. Radium is never used without a preliminary curettage or biopsy. All patients with uterine bleeding in whom cancer is not found and a hysterectomy not done are warned that the curettage may not cure them and that, if the bleeding continues, they should immediately report for further examination. We believe that this is of the greatest importance. During the past year we encountered four interesting but unfortunate cases in all of which the preliminary curettage was negative, one with cancer of the tube, another with granulosa cell cancer of the ovary and two with cancer of the body of the uterus. In one case of cancer of the body of the uterus, the tumor was localized and of an infiltrating type and therefore easily missed; the second, was in an elderly patient who had multiple uterine myomas easily recognizable at her first admission to the hospital. Two curettings failed to detect cancer, which at the time of the hysterectomy was opposite a submucous myoma.

During the last twenty-year period of the Gynecological Department of the Albany Hospital there have been four cases of cancer of the cervix complicating pregnancy, while the following is the first case of cancer of the body of the uterus complicating pregnancy.

CASE REPORT

Mrs. M. C., aged thirty-five, Italian, was first seen in the Albany Hospital, March 8, 1931, when she was delivered of her fifth child. This was a spontaneous delivery of a 6-pound, 13-ounce girl baby. Her puerperium was normal. She next presented

herself in the Out-Patient Department, Sept. 9, 1931, because she had not menstruated in two months. A diagnosis of uterine pregnancy was made.

Oct. 8, 1931, she was admitted to the ward of the Albany Hospital because of a miscarriage which had taken place at her home. The family physician and the ambulance interne actually saw the fetus and the placenta. The next day she had a diagnostic curettage because of profuse bleeding. At this examination the vagina

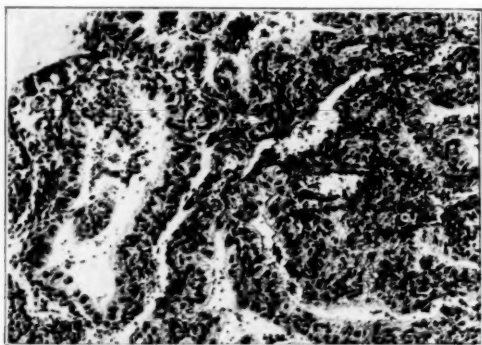


Fig. 1.—Postpartum endometrial fragment from the vicinity of the local tumor mass. It is histologically more malignant than the gross tumor. The glands are closely packed together, the epithelium shows much variation in size, shape, and staining density. Large atypical nuclei and an abundance of mitotic figures are in favor of its essentially neoplastic character. No decidua is to be seen.



Fig. 2.—The uterus opened showing the hemorrhagic tumor near the left cornu. The rest of the endometrium is quite smooth but with typical decidual and syncytial cells infiltrating it.

was found mildly relaxed, the cervix bilaterally lacerated and soft and patulous, and the uterus enlarged. A large amount of curettings was obtained. The pathologic examination of the curettings revealed a few microscopic foci of judged adenocarcinoma with decidual reaction elsewhere in the stroma. Oct. 14, 1931, a panhysterectomy, bilateral salpingo-oophorectomy and appendicectomy were performed under ether anesthesia by me. At operation the uterus was found enlarged

about two times, soft and freely movable. The tubes and ovaries were normal. A large corpus luteum was present in the right ovary. There were no evidences of metastases.

The patient made a normal convalescence and was discharged from the hospital Nov. 1, 1931. She has been followed in the Out-Patient Department and at the present time (April, 1933), is in good health.

Pathologic Report (V. C. Jacobsen, M.D.).—The specimen consisted of the uterus, tubes, and ovaries. The uterus measured 10 by 7 by 2.2 cm. The muscle wall was

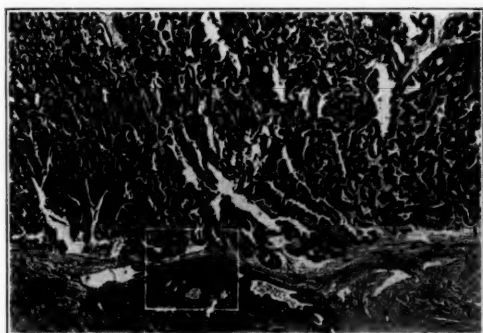


Fig. 3.—The endometrial tumor essentially a large polypoid mass, not histologically malignant in all fields. The square outlines an area in Fig. 4 where the wall is invaded slightly.

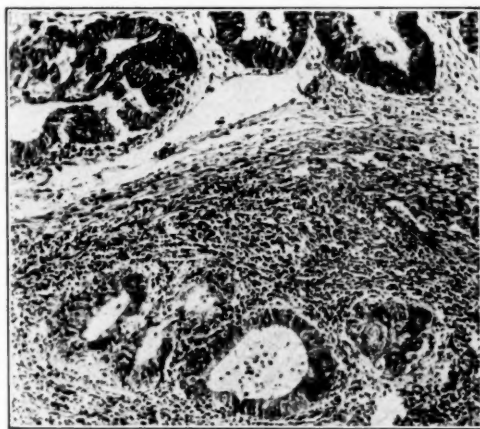


Fig. 4.—The field outlined in Fig. 3 showing invasion of the wall of the uterus with accompanying lymphocytic infiltration about the glands.

soft, congested, and blood vessels were very prominent. The serosa was not remarkable. On opening the uterus the endometrium averaged about 1 mm. in thickness. At the posterior surface near the opening of the left cornu was a dark-colored polypoid growth about 2 cm. in diameter, with a broad base about 1.5 cm. in width. The surface of this mass was somewhat ragged and presented smaller polypoid excrescences. In incising this, a tendency to friability of the superficial portion was noted, but a dense consistence was noted elsewhere. It was firmly adherent to the wall but there was no gross evidence of tumor invasion. There was marked congestion and some hemorrhage into the mass which resembled somewhat

placental tissue or even a choriocarcinoma in the gross. The rest of the endometrium was pale, fairly smooth and presented no gross abnormality. The cervix showed superficial laceration.

The fallopian tubes and ovaries appeared normal. A large corpus luteum was present in the right ovary.

Microscopic Examination.—A. The first tissue submitted was obtained by curettage Oct. 9, 1931, one day after the miscarriage. The fragments were fixed in Zenker's fluid and stained with hematoxylin and eosin. In most parts the endometrium was typical of pregnancy, with decidual reaction and syncytial cells in great number. Here and there, however, were fields in which the endometrial glands were different from those elsewhere, being more hyperplastic and in particular showing a drift from the normal nuclear pattern in their epithelium. Large hyperchromatic nuclei and mitoses were abundant. In Fig. 1 is a field from which the preoperative diagnosis of "probably adenocarcinoma" was made.



Fig. 5.



Fig. 6.

Fig. 5.—A field from one of the most cellular portions of the tumor. Closely packed, hypertrophied glands, with multiple layers of columnar epithelium, hyperchromatic cytoplasm and nuclei. The stroma is scant. This picture entitles the tumor to be called "adenoma malignum" or "adenocarcinoma."

Fig. 6.—The endometrium far removed from the tumor shows the typical picture of six days postpartum.

B. Sections taken from the hemorrhagic mass near the left cornu showed it to be composed of a dense growth of glands with relatively scant stroma (Fig. 3). The glands were of a very hyperplastic type as a whole but in places they were very closely packed together and the epithelium was distinctly atypical in type so that a diagnosis of malignancy seemed justified (Fig. 6). The picture was what Ewing would probably call "adenoma malignum." Mitoses were scarce. In the stroma were a few lymphoid cells. At the base of the growth invasion of the upper muscle layer has occurred and considerable lymphocytic infiltration was present (Fig. 4).

While the picture is not uniform throughout the tumor, it is probable that the whole mass is malignant, but generally of a low grade of malignancy. Some microscopic foci, however, more rapidly growing than others, display a giant reproduction of uterine glands and are lined by several layers of columnar cells.

Elsewhere in the uterus (Fig. 5) is the usual picture of postpartum endometrium with abundant syncytial cells and decidua. A few degenerated chorionic villi are found.

SUMMARY

A case is reported of adenocarcinoma of the body of the uterus associated with a four months' pregnancy. The diagnosis of cancer was made from fragments removed by curettage twenty-four hours after miscarriage. From a study of this incident, as well as our experience in the Gynecological Department of the Albany Hospital, the following conclusions may be drawn:

1. Every case of pathologic uterine bleeding should be considered as a possible cancer until proved otherwise.
2. Every patient with abnormal uterine bleeding excepting tubal pregnancy, threatened abortion, and infection should have either a diagnostic curettage or a hysterectomy.
3. All curettings should be examined microscopically, even though they appear nonmalignant.
4. In suspected cases of cancer of the body of the uterus where a panhysterectomy is not clearly indicated, the curettage should be done gently and just enough tissue removed for diagnosis by frozen section, so that the chance for dissemination of cancer cells can be reduced to a minimum.
5. If cancer can be so diagnosed, the curettage should be immediately followed by a panhysterectomy, or in poor operative risks by radium.
6. If the diagnosis cannot be made by frozen section, Zenker-fixed sections can be obtained in twenty-four hours by the technic employed in the Pathological Department of the Albany Hospital.
7. Radium is never used in cases of uterine bleeding without a preliminary diagnostic curettage or biopsy.
8. All patients with uterine bleeding in whom cancer is not found are warned that the curettage may not cure them and that, if the bleeding continues, they should report for further examination.

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A COMPARISON OF THE ASCHHEIM-ZONDEK AND THE FRIEDMAN TESTS IN NORMAL AND ABNORMAL PREGNANCY*

AN ANALYSIS OF THE LITERATURE AND A REPORT OF THE RESULTS
OBTAINED IN 1112 CASES

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THE hormonal relationships which form the basis of the Aschheim-Zondek test for pregnancy have received such adequate mention in the literature that further repetition is superfluous. The uniformly good results obtained with the original mouse method left little to be desired from the standpoint of accuracy. Although the original technic has been modified, the Aschheim-Zondek reaction in principle remains to date the only undisputed practical contribution to clinical practice which has come from the wealth of scientific facts gained through recent studies of female sex physiology. What it lacked in simplicity of technic and speed of reaction has been provided by the rabbit ovulation test, a modification based upon identical principles and first suggested by Friedman.^{1, 2}

The development of the Friedman modification of the Aschheim-Zondek test as a diagnostic procedure in pregnancy is due to the efforts of numerous investigators (Friedman and Lapham;³ Reinhart and Scott;⁴ Wilson and Corner;⁵ Schneider;^{6, 7, 8} et al.). Except for slight variations in technic proposed by each of these workers, the methods used are essentially the same and the results reported are strikingly uniform. Summaries of the methods advocated by various authors appear in the publications of Schneider;⁸ and Ware and Main.⁹ White and Severance¹⁰ have compared the accuracy of the original Aschheim-Zondek method with the Friedman modification in a series of 231 cases (Aschheim-Zondek, 191 cases; Friedman method, 40 cases).

The literature to date reports more than 8685 tests performed according to the Aschheim-Zondek technic. Table I summarizes the results reported by various authors; it includes only those series consisting of 100 or more tests. Approximately 1900 tests have been reported with the Friedman method. Table II summarizes these results.

The variations in the results reported by different investigators may be due to some extent to technical skill; the chief factor, however, appears to be the interpretation of the results obtained. It must be

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kept clearly in mind that this test is *not* a test for pregnancy per se, but a test for the hormonal response to the presence within the body of living fetal tissue in connection with the maternal blood stream.

TABLE I. RESULTS WITH ASCHHEIM-ZONDEK TECHNIC

AUTHOR	TOTAL NUMBER PA- TIENTS	PREGNANT PATIENTS		NONPREGNANT PATIENTS		AC- CURACY GROSS PER CENT
		PER CENT CORRECT POSI- TIVES	PER CENT FALSE NEGA- TIVES	PER CENT CORRECT NEGA- TIVES	PER CENT FALSE POSI- TIVES	
Aschheim ¹²	1007	98.2	1.7	99.3	0.75	98.8
Ehrhardt ¹³	3000					98.5
Lassen ¹⁴	1198	97.0	3.0	96.1	3.9	96.9
Wiesner ¹⁵	415					97.6
von Ammon ¹⁶	324					99.4
Parvey ¹⁷	370					98.5
Frank, Goldberger, and Felshin ¹⁸	350			100.0	0.0	96.9
Mazer and Hoffman ¹⁹	314	73.0	27.0	90.0	10.0	82.0
Jones and Mugrage ²⁰	255	99.0	1.0	96.0	4.0	97.6
Dodds ²¹	208	96.8	3.2	98.8	1.2	97.6
Becker ²²	250					98.0
Kuga ²³	179	100.0	0.0	100.0	0.0	100.0
White and Severance ¹⁰	191	99.0	1.0	93.0	7.0	90.0
Brühl ²⁴	180	98.6	1.4	95.0	5.0	96.8
Bland, First, and Roeder ²⁵	200	82.4	7.6	93.0	7.0	93.0
Davis and Walker ²⁶	143	96.0	4.0	100.0	0.0	98.0
Wahl ²⁷	129	98.9	1.1	100.0	0.0	99.3
Mack ²⁸	100	100.0	0.0	97.2	2.8	99.0
Stewart ²⁹	101					99.0

Total cases, 8685; Average accuracy, 96.6 per cent

The source of the hormone present in the urine is still disputed, there being good evidence in favor of the contention (Philipp,^{30, 31} Fels,³² Collip³³) that it is produced by the products of gestation themselves, and not solely by the anterior lobe. Regardless of source, death of the ovum and its elements (trophoblast, placenta) soon leads to failure of hormone production and a negative Aschheim-Zondek reaction, as in cases of incomplete abortion, missed abortion, tubal abortion, etc. A positive test in these cases signifies a continuance of the biologic connection between living fetal elements and the maternal circulation.

Since a positive reaction can be obtained only when the living chorionic elements (normal or pathologic) are in contact with the maternal blood stream, negative tests in cases of interrupted pregnancy cannot properly be classed as false negatives as appears in the publications of certain workers. White and Severance,¹⁰ for example, report a gross error of 10 per cent; excluding in their series the negative reaction obtained in cases of interrupted pregnancies (intra- and extrauterine), this error is reduced to 3.7 per cent. Aschheim¹² and Zondek in evaluating their results calculated only the false reactions (1.2 per cent) obtained from the urine specimens of patients known definitely to have been normally pregnant or not pregnant.

Without deducting these "false negatives" the average accuracy with the original method in the 8685 cases summarized above exceeds 96 per cent, even including the unusually poor results (82 per cent accuracy) reported by Mazer and Hoffman.¹⁹

TABLE II. RESULTS WITH FRIEDMAN MODIFICATION

AUTHOR	TOTAL NUMBER PATIENTS	PREGNANT PATIENTS		NONPREGNANT PATIENTS		ACCURACY GROSS PER CENT
		PER CENT CORRECT POSITIVES	PER CENT FALSE NEG- ATIVES	PER CENT CORRECT NEG- ATIVES	PER CENT FALSE POSITIVES	
Friedman and Lapham ³	92	100.0	0.0	100.0	0.0	100.0
Reinhart and Scott ⁴	150					98.7
Schneider ³⁴	400	98.5	1.5	99.0	1.0	98.8
White and Severance ¹⁰	40	82.0	14.0	100.0	0.0	97.5
Magath and Randall ³⁵	85	97.0	3.0	98.0	2.0	97.7
Davis and Walker ²⁶	65	97.0	3.0	96.0	4.0	97.1
Parache ³⁶	180	100.0	0.0	100.0	0.0	100.0
Stricker ³⁷	75	100.0	0.0	100.0	0.0	100.0
Dorn, Morse, and Sugar- man ³⁸	150			100.0	0.0	97.5
Martins ³⁹	100	100.0	0.0	100.0	0.0	100.0
Bradford and Todd ⁴⁰	22	100.0	0.0	100.0	0.0	100.0
Beasley ⁴¹	52	100.0	0.0	100.0	0.0	100.0
Wilson and Corner ⁵	196					99.5
Ware and Main ⁹	100	98.5	1.5	100.0	0.0	99.0
Mazer and Ziserman ⁴²	182	92.0	8.0	95.0	5.0	93.5

Total cases: 1899; average accuracy: 98.5 per cent

The results obtained with the rabbit ovulation method of Friedman are strikingly uniform considering the fact that the technics employed vary considerably, differing not only as to the amount of urine injected in one or several doses, the types of rabbits utilized (adult, immature), and the time which elapsed between the injection and the reading of the test. The uniformly good results seem to indicate that these variations in technic are of little significance in determining the accuracy of the method.

Our experience with these hormone tests in the diagnosis of pregnancy covers a period of about three and one-half years. Since our first report²⁸ of the results obtained in 100 cases with the original method in 1930, we have performed these tests in more than 1400 additional cases. Since May, 1931, we have discontinued the use of the original technic in favor of the Friedman modification. The accuracy of these tests is definitely known in the series of 1112 cases which form the basis of this report.

Our material consists almost entirely of cases referred to us by a large group of physicians engaged in private and clinic practice, the urine specimens being submitted for the most part without clinical data. In order to determine the comparative accuracy of these two methods in our hands, it was necessary to ascertain by means of subse-

quent questionnaires the results obtained and the clinical data known only to the physician who referred the urine for diagnosis. This series, consisting as it does almost entirely of unknown cases, demonstrates the practical value of the test uninfluenced by any subjective bias.

In our series of 1112 tests in which the accuracy has been definitely determined, the original Aschheim-Zondek technic was followed in 546 cases, and the Friedman method in 466 cases. These were divided into three groups according to clinical outcome:

1. Normal pregnancy	521
2. Not pregnant	530
3. Abnormal or interrupted pregnancy	61

TABLE III. NORMAL PREGNANCY

	ASCHHEIM-ZONDEK METHOD		FRIEDMAN METHOD	
	CORRECT POSITIVES	FALSE NEGATIVES	CORRECT POSITIVES	FALSE NEGATIVES
Fifth week	26	1	21	
Sixth week	26		58	1
Seventh week	21		31	1
Eighth week	24		29	1
Ninth week	8	2	2	
Tenth week	20		8	
Eleventh week	13	1		
Twelfth week	8	1	8	
Twelfth week plus	13	2	9	1
Unknown	87		96	2
	246 (97.3%)	7 (2.7%)	262 (97.8%)	6 (2.2%)

1. *Normally Pregnant Patients.*—This group includes only those tests performed upon patients subsequently ascertained to have been normally pregnant. Urine specimens were submitted for examination from the early weeks of pregnancy (in 5 cases on the second day of gestational amenorrhea) to full term. In 48 cases the urine was examined within one week following the expected date of the first missed period; one false negative reaction was obtained in this group (Aschheim-Zondek technic). The highest degree of accuracy appears to result during the early months of pregnancy, due possibly to the fact that greater amounts of hormone are excreted during this period (Zondek).⁴³

Table III shows the results obtained with both methods in cases of normal intrauterine pregnancy. There appears to be little difference in the accuracy of both methods. The slightly greater accuracy of the Friedman method lies undoubtedly in simplicity of technic. Mortality and morbidity of mice is an important source of error in the original method. Frequently only one of the 5 mice originally injected at the beginning of the test survived the hundred-hour period, particularly when the urine was toxic and during the hot summer months. Other

workers have reported a mortality of 7 to 20 per cent among the mice. In such cases the result was always doubtful when no ovarian changes were noted, since not infrequently several mice of a group failed to react to the hormone, whereas the remainder showed strongly positive reactions. Zondek's method⁴⁴ of treating toxic specimens by detoxifying with ether was useful in urine samples known to have a toxic effect, although this property of the urine was never discovered until a trial test had resulted in the death of the animals. Much valuable time was thereby lost until the test could finally be completed. Toxicity of the urine rarely causes death of rabbits. The ether method of detoxification has been found useful on several occasions in treating the urine of patients suffering from pyelitis.

TABLE IV. NONPREGNANT PATIENTS

	ASCHHEIM-ZONDEK METHOD		FRIEDMAN METHOD	
	CORRECT NEGATIVES	FALSE POSITIVES	CORRECT NEGATIVES	FALSE POSITIVES
Amenorrhea	203	4	201	3
Menopause	16		26	
Myoma	8		6	
Ovarian cyst	10		6	
Salpingitis	7		9	
Pelvic malignancy	10		5	
Pituitary tumor	2		2	
Brain tumor and amenorrhea				1
Normal male	3			
Normal female	3			
Pseudocyesis			5	
	262 (98.5%)	4 (1.5%)	260 (98.5%)	4 (1.5%)

H. *Nonpregnant Patients.*—This group was composed of patients not considered to have been pregnant by the physician to whom the report was made. In several instances, however, particularly in cases which are recorded as having given false positive reactions (functional amenorrhea), the possibility of early, unrecognized abortion could not be ruled out with certainty. This series includes numerous endocrine cases and pelvic malignancies, although the majority represent cases of delayed menstruation associated with pelvic disorders where early pregnancy was to be excluded. Reaction I (Aschheim-Zondek method) was frequently obtained in cases of pelvic malignancy. These cases, for the most part, were receiving deep roentgen irradiation.

Table IV again shows how nearly both methods approach each other in accuracy. The degree of accuracy obtained in nonpregnant patients is somewhat greater than that obtained in pregnant patients (i.e., fewer false positives than false negatives).

III. *Abnormal or Interrupted Pregnancies.*—This group includes cases of threatened and incomplete abortion, missed abortion, fetal death (near term), tubal abortion, unruptured tubal pregnancy, hydatidiform mole, malignant chorionepithelioma, and urine specimens from patients less than one week postpartum.

The reactions obtained in cases of interrupted pregnancy (intra- and extrauterine) were variable and depended upon the length of time which had elapsed since the fetal elements lost their connection with the maternal blood stream. This explains the occurrence of both positive and negative reactions in cases of incomplete abortion, tubal abortion, and fetal death. It is important that laboratories performing these tests in cases submitted for the diagnosis of extrauterine pregnancy, particularly, stress the fact that a negative reaction does not exclude the possibility of a dead tubal pregnancy. Similarly a positive reaction does not exclude the possibility of intrauterine fetal death, since elimination of the hormone may continue for a time, as evidenced by the postpartum positive tests noted in Table V. When

TABLE V. ABNORMAL OR INTERRUPTED PREGNANCY

	ASCHHEIM-ZONDEK METHOD		FRIEDMAN METHOD	
	POSITIVE	NEGATIVE	POSITIVE	NEGATIVE
Abortion	2	4	1	1
Missed abortion		1		3
Fetal death near term	1		1	
Tubal pregnancy	4	1	6	3
Hydatid. mole	4		7	
Chorionepithelioma	6		12	
Postpartum 2-7 days	4			
	21	6	27	7

tubal pregnancy is suspected a positive test in the presence of a tubal mass is strong presumptive evidence of tubal pregnancy. A negative reaction signifies that even if an ovum is present it is no longer alive or capable of further invasion. The practitioner must understand the hormonal significance of the reaction and, in the last analysis, must depend upon his clinical judgment in evaluating the laboratory findings in abnormal cases. It must be emphasized again that this reaction is not a test for pregnancy per se but a demonstration of the hormonal response within the body to the presence of living fetal elements.

Hydatidiform Mole.—Five cases of hydatidiform mole have been available for study. Positive tests were obtained with both methods at the time of expulsion and as long as six months following expulsion. The amount of hormone present in the urine was in most instances so great that positive tests could be elicited with urine quantities much smaller than those necessary to provoke a test in normal pregnancy. This titration effect, described by numerous investigators (Rössler,⁴⁶ Zondek,⁴⁵ Mack and Catherwood,⁴⁷ et al.) serves to differentiate hyda-

tidiform mole from normal pregnancy. The persistence of a positive reaction after expulsion of the mole necessitates a guarded prognosis since it may signify retained mole tissue or malignant chorionic degeneration. In the absence of clinical symptoms (uterine bleeding) a positive reaction which may persist for several months (in one case as long as six months) does not necessitate surgical intervention. If, however, bleeding occurs in the presence of a positive test, immediate curettage should be performed to rule out chorionepithelioma. The persistence of a strongly positive test four months after expulsion of a mole was noted in one case with large bilateral lutein cysts of the ovary.

Malignant Chorionepithelioma.—Four cases of chorionepithelioma, two of which have previously been reported,⁴⁷ have been tested. As in cases of hydatidiform mole, such high concentrations of hormone are present in the urine that positive tests can be obtained with minimal amounts of urine. Three of our cases were preceded by mole pregnancies, and one by a criminal abortion one and one-half years previously. All cases have been carefully tested over long periods by either the Aschheim-Zondek or Friedman test. Three patients are apparently alive and free from recurrence after hysterectomy and postoperative irradiation. The urine subsequently has consistently given negative tests. The urine of one patient with an advanced chorionepithelioma continued to give strong positive reactions after complete hysterectomy and intensive irradiation. She developed vaginal metastases which were removed surgically, followed by radium implantation at the site of operation. She disregarded advice to continue treatment and left the city. Her urine still provoked a strongly positive Aschheim-Zondek reaction. A follow-up investigation revealed that she died six months later, supposedly of metastases. One case of chorionepithelioma testis gave a positive Aschheim-Zondek test two months after surgical removal. The patient then received deep x-ray therapy after which the test became negative. He is apparently free from recurrence.

SUMMARY

An analysis of the literature on hormone tests for pregnancy and our own experience with 546 Aschheim-Zondek and 566 Friedman tests demonstrates a high degree of accuracy for both methods, the latter being slightly more accurate as well as easier and quicker.

In proved cases of normal pregnancy we obtained an accuracy of 97.3 per cent with the Aschheim-Zondek test and an accuracy of 97.8 per cent with the Friedman method.

In patients definitely determined not to have been pregnant we obtained an accuracy of 98.5 per cent with both methods.

In abnormal or interrupted pregnancy the result of the test should be interpreted with the clinical findings, a negative test signifies either

a nonpregnant state or an interrupted pregnancy, a positive test strongly indicates living fetal elements, but due to a temporary persistence in elimination of the hormone, recent interruption or fetal death cannot be excluded.

In cases of hydatidiform mole and malignant chorionepithelioma, the amount of hormone excreted is many times greater than that excreted during normal pregnancy. The persistence of positive tests after treatment of these neoplasms strongly suggests continued chorionic proliferation.

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TWO FATAL CASES OF HYPEREMESIS GRAVIDARUM WITH RETINAL HEMORRHAGES

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THE occurrence of hemorrhages in the retina in association with pernicious vomiting of pregnancy must be either extremely uncommon or this finding is overlooked. The latter conclusion may have been true many years ago but in recent years the ophthalmoscope has become part of the armamentarium of the obstetrician. Ophthalmologic consultants are readily available; the visual symptoms are so pronounced that retinal examination is immediate and the picture must become manifest.

A description of two unusual cases and the pertinent necropsy findings are here given:

CASE 1.—A. M., a para i, gravida ii, twenty-two years old, was admitted to Sloane Hospital February 24, 1931, for hyperemesis. The date of her last menstrual period was November 22, 1930; the expected date of labor, August 29, 1931. The histories of her past and present pregnancies were extremely interesting. Three years previously she had had a stillbirth at seven months. This pregnancy had been complicated in the last three or four months by severe vomiting, weight loss of 30 pounds, severe headaches, and, in the last few days before delivery, jaundice. She also had "kidney trouble," that required cystoscopy. Following delivery she recovered readily, had no symptoms pointing to the genitourinary tract, and remained well until one month before admission. Her present illness began with vomiting, at first only in the morning, and on January 26, 1931, after each meal. She lost 15 pounds. Jaundice had been noticed one week before admission. Hematemesis had occurred three times three days later. One day before coming into the hospital she had developed "pain in the back" and "burning" on micturition. Headaches had been present every morning; these had disappeared later in the day. No visual disturbance, abdominal pain, edema of face, hands and feet, or paresthesias had been noticed.

The past history was negative except for an attack of pneumonia in 1925.

Physical Examination: The patient was a well-developed white female of twenty-two, who was slightly jaundiced, showed evidence of loss of weight, and appeared seriously ill. Eyes were sunken, sclerae icteric, and the conjunctivae clear. Some dried blood was present in both nostrils. Ears were normal. Lips were dry and fissured. There was a marked odor of acetone on the breath. The tongue was dry and red. The teeth had had considerable dental work. The pharynx was injected. The tonsils had been removed. The examination of the neck was negative. The lungs showed no abnormal changes. The heart was of normal size, the apex beat being felt in the fifth interspace, 9 cm. to the left of the midsternal line. The sounds were regular, of good quality, rate 120, and there was a soft, blowing systolic murmur in the second and third interspaces to the left of the sternum. The skin of the abdomen was inelastic, dry, and wrinkled. The abdominal movements were unrestricted. The liver was not felt because of marked tenderness in the right upper quadrant, but was percussed 10.5 cm. below the costal margin in the right parasternal line. The spleen was

not enlarged and was not palpable. There was marked tenderness in each costo-vertebral angle. The kidneys were not palpated. There was considerable generalized abdominal spasm which, although it seemed voluntary, could not be overcome. The extremities were normal except for marked tenderness in each calf and a small ecchymosis on the lateral surface of the right arm where a hypodermic injection had been given previously. A pelvic examination showed the uterus to be the size of a two and one-half months' pregnancy.

Temperature 99.8° F., respiration 24, blood pressure 80/50.

A diagnosis of pregnancy, hyperemesis gravidarum, pyelitis, and toxic hepatitis was made on admission.

Although the patient was considered extremely ill, it was felt that termination of the pregnancy at this time would be disastrous and it was decided to force fluids, glucose, and saline. The next day the condition showed definite improvement. The following day the urinary output was almost 1500 c.c. Vomiting had not occurred in twenty-four hours. Hepatic tenderness was no longer present. The pulse was 100. Improvement continued and seven days after admission the pulse rate had fallen to 84. There had been no vomiting of food for four days. Tenderness, however, persisted in both costovertebral angles. A low-grade fever, reaching 101° F. on three occasions in the first two days, had gradually subsided by the fifth day. On the evening of March 6, 1931, the eleventh day of hospitalization, the patient complained of "blurry" vision. The next morning she seemed drowsy but was easily aroused; she stated that she "felt sleepy" and that her vision was still blurred. The pulse had for three days previously fluctuated between 90 and 116. Examination disclosed: Slight resistance but not true rigidity of the neck, bilateral Kernig's sign, more marked on the right, and positive Oppenheim on the right. The discs were hazy; and a papilledema about 1.5 diopters was observed, together with large fresh flame-shaped hemorrhages in both retinas that were confined to the region of the optic nerves only. A spinal puncture revealed clear fluid, not under increased pressure, having 9 cells, all lymphocytes, per cubic centimeter; globulin and glucose were present in normal amounts. A dilatation and curettage was done a few hours later under gas and oxygen anesthesia. Following operation fluids were forced and a transfusion was given; the urinary output was uncertain because of incontinence but seemed decreased. A positive Babinski's sign appeared on the left and a bilateral ankle clonus developed. A small hemorrhage was noticed in the posterior superior quadrant of the right ear drum. Coma gradually supervened. The pulse reached 160, and the temperature 106.4° F., on the thirteenth day when death ensued.

A postmortem examination showed the following essential findings:

Anatomical Diagnosis: Suppurative cholecystitis, cerebral hemorrhages, miliary focal necroses of the brain, obsolete pyelonephritis, acute pyelonephritis, puerperal uterus, corpus luteum of ovary, acute cystitis.

The liver weighed 1705 grams and measured 28 by 17 by 7 cm. Glisson's capsule was grey, smooth, and of normal thickness. On section the cut surface was reddish brown in color. The blood vessels and bile ducts showed no gross changes. The lobulations were distinct.

The surface of the gallbladder was grey and greenish in color. The wall was of normal thickness. It contained approximately 60 c.c. of blackish green bile. The mucosa was soft and honeycombed. None of the bile ducts was obstructed.

The left kidney weighed 135 grams and measured 11.6 by 5 by 3.4 cm. The right kidney weighed 95.5 grams and measured approximately 10.5 by 5 by 3.2 cm. The capsule stripped easily. Fetal lobulations persisted, and there were several depressed scars less than 1 cm. in diameter. On section the cortex was thin

in the region of the scars but was of approximately normal thickness elsewhere. The kidney substance was slightly paler than normal. The striations were distinct. The glomeruli appeared as tiny granules. The pelves had numerous tiny injected vessels, more marked on the right. The ureters and bladder were normal.

The brain was edematous and a few small areas of hemorrhage were found in the cerebral peduncles.

Histologic Examination—(gallbladder): The submucosa and muscle layers were markedly edematous. Fibrin was present and polymorphonuclear leucocytes were found in these two layers though not in great numbers. Bacteria could not be demonstrated with either Gram's or Levaditi's stains.

The kidneys showed numerous scars throughout the cortex. The tubules had been obliterated in these areas and the glomeruli lay close together. Some of the glomeruli had become fibrosed. About others in which the capillary loops were still permeable, the capsule of Bowman was thickened and hyaline. The sacs were densely infiltrated with lymphocytes among which were a few eosinophiles. Between the scars the tubules and glomeruli were normal. Some of the tubules were dilated, others contained polymorphonuclear leucocytes. The interstitial tissue was infiltrated by many lymphocytes. In the stroma beneath the mucosa were many dilated capillaries, some compact fibrin, and many lymphocytes together with a moderate number of eosinophiles. Hemorrhages were present in the peripelvic fat.

Some of the chief cells of the anterior lobe of the pituitary were larger than normal.

In the sylvian fissure of the temporal cortex, the pia was thickened, especially in the fissure, where one of the larger vessels was seen to be partially thrombosed. The blood vessels were all engorged, and there were many erythrocytes in the pial meshes. The cortex and white matter showed engorgement of their vessels.

Striatum and Internal Capsule: A. There was some reduplication of the cells of the ependymal lining with a mild subependymal increase of astrocytes and microglia. There were a number of varying sized hemorrhages in the striatum nearest the ventricle. Some were ring hemorrhages about vessels. There seemed to be an increase of small vessels in this area, some degeneration of the striatal ganglion cells, and a hypertrophy of some of the astrocytes. B. Here only a very few of the perivascular hemorrhages were found.

Midbrain: There was quite an increase in the subependymal glia in one side of the aqueduct of Sylvius, many little glia rosettes being found. Just above this in the roof of the aqueduct was a zone of spongy tissue in which there were quite a number of small hemorrhages, some perivascular. There was a great increase of small blood vessels here, many of which had somewhat thickened walls. There were similar changes in the floor of the aqueduct. Many of the large ganglion cells of the fourth nerve nuclei bilaterally showed varying stages of simple degeneration, although some seemed well preserved.

CASE 2.—G. G., white, para 0, gravida ii, aged twenty-one years, was admitted to Sloane Hospital September 9, 1931, because of severe vomiting of one month's duration. The date of the last menstrual period was June 18, 1931; the expected date of labor, March 25, 1932. Her previous pregnancy had been terminated in the second month, July 22, 1930, because of severe vomiting and loss of weight. The interval history was negative.

About the fourth week of the present pregnancy she began to have severe nausea and vomiting. The severity gradually increased so that no solid food could be retained. Constipation was marked, and enemas were necessary. Headache was present but, apparently, not extreme. There were no visual disturbances, symptoms of genitourinary disturbances, or paresthesias. A loss of about 30

pounds in weight had occurred. Her past history, except for epistaxis at irregular intervals, was entirely negative. Her mother had died at the age of twenty-six in "childbirth" and no details were known by the patient. Her father was in "fair" health. There were no known cases of tuberculosis, renal disease, heart disease, diabetes, hemophilia, or purpura in the familial history.

Physical Examination.—A well-developed white female of twenty-one who was drowsy and showed signs of recent loss of weight. The skin was warm and dry and not icteric. The conjunctivae were of good color. The tongue was thickly coated. The eyes, ears, sinuses, neck, chest, lungs, were entirely negative. The heart rate was 88 and sounds were of good quality. The liver, spleen, and kidneys were not felt and were not tender. The uterus was palpable 4 cm. below the umbilicus. The extremities were negative except for some loss of muscle tone and loss of fat. The blood pressure was 80/60, temperature 99.2° F., pulse 88, respiration 22.

She was considered a case of hyperemesis gravidarum of moderate severity. Food and fluids were withheld per os and fluids, glucose, and saline, were administered subcutaneously and intravenously. The pulse rate reached 134 on the second day and then subsided in sharp variations to 80 on the sixth day. The urinary output was 1400 c.c. on the second day and continued over 1500 c.c. each day until the fifth day when all intravenous and subcutaneous administrations of fluid were discontinued. The temperature was 100.2° F. on several occasions until the sixth day, when it became normal. High carbohydrate fluids, ginger ale, orange juice, grape juice, carbonated water, were started by mouth on the third day, and were retained with but slight difficulty, only small amounts being regurgitated. Hypodermic injections of sodium luminal were used in varying amounts as sedative. Apparent improvement continued until the twelfth day after admission when it was noted that the gums were oozing blood from the interproximal spaces. This was swallowed and would precipitate vomiting. The pharynx was reddened and covered with small aphthous ulcers. The gingival margins were cauterized with silver nitrate and a transfusion (500 c.c. of blood) was given. The next night her temperature rose to 102° F. The following morning some bleeding occurred from the right naris. Purpuric areas were present in both thighs where hypodermic injections had been given. Several hours later some oozing occurred from the left naris. About this time, September 24, 1931, she first complained of blurred vision. The retinas had been examined on admission and were found to be normal. Reexamination was done at once and nothing abnormal could be detected. An examination on September 26, revealed only slight edema and blurring of the discs. No retinal hemorrhages were present. Inability to focus the eyes was the next complaint. No obvious muscular defects were found and a general neurologic examination was negative. Two days later, September 28, the patient was drowsy but cooperative and rational. Horizontal nystagmus was present on gaze to the left and right (rapid to right, slow to left). The heart rate was 120; the lungs were clear; the liver edge was palpable 3 cm. below the costal margin, and was not tender. Numerous ecchymotic areas of previous hypodermoclyses and infusions were present; bilateral clonus, but no Babinski reflex was elicited. There was blurring of both retinal discs, more marked on the temporal side of the left disc and uniformly distributed on the right. In the right fundus adjacent to the disc was a recent hemorrhage. The veins were full and their appearance suggested the oozing of blood into the sheaths of the vessels. Because of the tachycardia, hemorrhagic tendency, and outcome of the previous case that this was beginning to resemble, it was decided not to interrupt the pregnancy. The same evening tenderness in each costo-vertebral angle was discovered. Repeated examination of the eyegrounds revealed

new retinal hemorrhages confined to the discs, marked edema of the retina, uneven in its distribution, was present surrounding the discs, and the fundus picture was indicative of a toxemia. Coma supervened. A divergent strabismus and a right Kernig's sign appeared. Tenderness persisted in the costovertebral angles. The heart rate increased to 150. The temperature rose from 102.6° to 107° F. just before death.

Autopsy No. 10,798, History No. 312,698. Only the important data will be given:

Anatomic Diagnosis.—Pregnancy; cortical necrosis of kidneys; fatty liver; petechial hemorrhages in brain, epicardium, endocardium, and pleurae; fibrous pleural and peritoneal adhesions.

Liver: Weighed 1540 grams and measured 26 by 19 by 4 cm. The capsule was quite smooth and shining. The left lobe was congested. The cut surface appeared pale yellow. No obvious necrotic changes were seen. The lobulations were quite distinct.

Liver (microscopic): The capsule was apparently normal. Throughout the parenchyma the liver cells in the neighborhood of the efferent veins were swollen, contained fat vacuoles, brownish tan pigment, and stained a pale pink. The nuclei in these areas had lost their normal staining reaction. Pyknosis and karyorrhexis had occurred. Some cells were without any trace of a nucleus. The cytoplasm was granular and homogeneous. The bile ducts were normal.

Kidneys: The right kidney weighed 130 grams and measured 11.5 by 7 by 2.5 cm. The organ was soft and flabby. The capsule stripped easily, leaving a smooth and shining surface. Beneath the capsules could be seen large areas of congestion and hemorrhage. Over the lower pole this discoloration was especially prominent, making it appear almost uniformly red. On section the cortex was of normal width. Congestion was marked and appeared in parallel striations, perpendicular to the surface of the cortex. Glomeruli were readily seen. There were several large hemorrhages in the submucosa of the pelvis. In the cortex were large areas that were opaque, dull, and yellowish white in color. The portion of such just beneath the capsule showed striations clearly, and glomeruli could be seen. Here, too, were thin lines of hemorrhage occurring at right angles to the surface. At the lower pole and to a lesser extent at the upper pole a narrow diffuse hemorrhage extended the entire width of the cortex. In the opaque areas the striations were obscured and the glomeruli could not be discovered.

The left kidney weighed 120 grams and measured 11 by 6 by 2 cm. It presented essentially the same features as the right, except that the changes appeared to be more advanced. The ureters were patent and appeared normal.

Kidney (microscopic): A fibrinous exudate was present on the surface. The majority of the cortex was necrotic and a great area showed coagulation necrosis; extensive hemorrhages had occurred into it. At the border tubules could be seen, one end of which was lined by apparently normal epithelium; at the other end of the tubule the epithelium was necrotic. The parenchyma of the medulla, which retained more of the normal characteristics, showed edema of the interstitial tissue with hemorrhages, swelling of the epithelial cells of the tubules, and in places granular degeneration of the cytoplasm. There was an absence of polymorphonuclear leucocytic reaction at any place. The pelvic mucosa could not be seen but a rather large hemorrhage had occurred into the peripelvic fat. Within several of the larger areas of hemorrhage in the cortex were small arteries. Red blood cells were within the lumina, and appeared also between the intima and media, in places almost completely separating these two structures. The erythrocytes were quite pale, and no fibrin could be found.

Elastic tissue stain: The internal elastic lamella of many small arteries was in places necrotic and actual rupture had occurred. At these places the media beneath was also necrotic, swollen and ruptured. Through these openings red blood cells poured in great numbers and lay in the surrounding parenchyma. Occasionally, the media was more or less intact and red blood cells appeared between the internal elastic membrane and the media, stripping the former from the latter.

Phosphotungstic acid stain: A. No fibrin was seen in the areas of hemorrhage.

B. In another section was an area of coagulation necrosis extending practically the full width of the cortex. The tubules were quite uniformly affected save in the patches noted above. Hemorrhage was not as marked but was nevertheless conspicuous. In the medulla edema and hemorrhage were found and the tubules presented the same alterations as described in the other section. The pelvic blood vessels were congested and dilated.

Gram stain: No microorganisms were seen. Fibrin was not found.

Fat stain: Fat was present occasionally in the epithelium of the convoluted tubules.

Brain: The scalp and calvarium showed no abnormalities. The dura and cerebral sinuses appeared normal. The cerebral hemispheres were symmetrical. The pia was smooth and translucent throughout. The gyral pattern was of moderate complexity. The pial vessels were moderately hyperemic. In the left postcentral gyrus 0.5 cm. from the superior longitudinal fissure was a small, round, softened depression in the cortical surface, showing on its base firm hemorrhagic mottling. There was also found hemorrhagic mottling of the precentral gyrus on the left in the region of the left paracentral lobule. This area measured 1.5 cm. in diameter. A similar symmetrical hemorrhage was seen in the corresponding location in the right paracentral lobule.

Over the anterior portion of the pons the tegmentum was hyperemic, especially below the floor of the fourth ventricle, extending down as far as the lower third of the medulla. Punctate hemorrhages were seen here in the inferior colliculus, in both portions of the chiasm on each side of the midline, in the medial nuclei of each thalamus, and just beneath the ependyma of the third ventricle. Hemorrhages were also found in the massa intermedia. The subpial hemorrhages described in the paracentral lobules above extended into the superficial layers of the cortex. In the posterior portions of both superior parietal lobules were a few tiny cortical hemorrhages, averaging 1 mm. in diameter. The small softened area noted externally in the left central gyrus was seen as a narrow zone of softened cortex.

Histologic Examination.—Cortex: A. The pia was slightly edematous and there were a number of small subpial hemorrhages. The pial vessels were engorged and the walls of some of the arteries slightly thickened. There were two large and several smaller hemorrhages in the outer two-thirds of the cortex. The parenchyma directly about the hemorrhages was somewhat edematous and showed a considerable loss of ganglion cells; some of those remaining were degenerative. The blood vessels in this zone showed slight thickening of their walls and a number of perivascular extravasations of red blood cells and serum.

Phosphotungstic Acid Stain: There was no astrocytic reaction.

Elastic Tissue Stain: Occasional small pial arteries and a number of the smaller cortical arteries showed thickening of their medial layers and, in some instances, considerable thickening of the intima. The elastic lamellae of these vessels had for the most part disappeared.

B. The pia and cortex here presented the same changes as above except for more numerous cortical hemorrhages.

Phosphotungstic Acid Stain: Showed no glial reaction.

Elastic Tissue Stain: Showed the same vascular changes as previously described.

Junction—Midbrain and Pons: In the tegmentum, beneath the floor of the ventricle were many small hemorrhages, some of which were perivascular. There was a mild subependymal edema and an increase of astrocytes in the roof of the ventricle with a small hemorrhage in one lateral area. The margins about a dilated perivascular space were edematous and there were a few large mononuclear cells. Some of these cells contained granular yellow pigment.

Phosphotungstic Acid Stain: The glial fibers in the roof of the ventricle were increased in number.

Elastic Tissue Stain: Vascular changes were found similar to those in the cortex.

Medulla: There were many small hemorrhages in the floor of the fourth ventricle in the region of the dorsal vagus and vestibular nuclei. Many of them were perivascular and in the walls of some of the vessels masses of fibrin could be seen. Mild edema was present in this area. There were cell losses in the twelfth dorsal vagus and vestibular nuclei bilaterally, the most marked losses being in the vagus group.

DISCUSSION

The two cases present some features that may possibly aid in evaluating the course of future cases.

Both patients on entrance to the hospital showed the results of severe persistent hyperemesis. They had lost considerable weight (15 pounds and 30 pounds), had low-grade fever (99.8° and 99.2°), and had hypotension (80/50 and 80/60). A similar history of severe vomiting in a previous pregnancy in the two instances terminated disastrously for the fetus (seven months' stillbirth and two months' therapeutic abortion). Under recognized therapy, there was a temporary clinical improvement in each patient. The next incident in both cases was blurring of vision and shortly afterward diplopia. Tachycardia was noted in conjunction with the onset of visual disturbances in one case; had occurred prior to it in the other. In Case 2, epistaxis, bleeding gums, and ecchymotic areas about hypodermic injections were present.

The laboratory tests were of no aid except to indicate the gravity of the condition. The changes in the urine and blood chemistry were those that may be found in any case of hyperemesis gravidarum. The blood pictures were those of a moderate secondary anemia; bleeding time, coagulation time, platelet count and fragility, were normal.

The etiology must remain unknown at present. The following facts must stand out. Lesions of the kidneys were found in the two instances, and in Case 1 there was an infectious process in the kidney and a severe suppurative inflammation in the gallbladder.

Retinal hemorrhages, occurring in patients having hyperemesis gravidarum seem all important when viewed in the light of Stander's article,* but when considered with the previously mentioned necropsy findings they are, as in many other diseases, only an expression of more profound processes in the brain. These lesions are not characteristic of hyperemesis gravidarum alone. Lesions similar to those presented by our patients have been found in pregnancy, though chiefly in many other con-

*Stander, H. J.: Surg. Gynec. Obst. 54: 129, 1932.

ditions that were not related to pregnancy. Alpers, in 1928, mentions like lesions occurring in phosgene poisoning, carbon-monoxide poisoning, grippe, pneumonia, typhus fever, encephalitis, cerebral tumor, arsphenamine poisoning, pernicious anemia, meningococcus meningitis, tuberculous meningitis, bronchopneumonia, erythema multiforme, psoriasis, malaria, scurvy, chronic nephritis, acute rheumatic fever, and meningovascular syphilis. De Vries described a case of eclampsia in which petechial hemorrhages were found only in the cerebral cortex. Some of the lesions described in chorea of pregnancy also fit into this same large group.

It seems reasonable and logical to suggest that the etiologic factor in both of our patients was not hyperemesis gravidarum per se. The existence of a severe infection in the kidney and gallbladder of the first patient and of an atypical cortical necrosis of the kidney of the second patient should be sufficient to produce severe vomiting; in the presence of a pregnancy a pernicious cycle could easily be established.

To attribute the hemorrhages to the entity, "hyperemesis gravidarum" and to disregard the underlying factors does not seem logical, especially when we consider the rarity of the condition and the existence of a similar hemorrhagic disturbance in diseases in which like renal and other lesions have been found.

CONCLUSIONS

1. Two fatal cases of hyperemesis gravidarum are reported in which hemorrhages were found in the retinas.
2. The retinal hemorrhages were a concomitant of multiple cerebral hemorrhages.
3. The finding of retinal hemorrhages is of serious prognostic omen and demands immediate termination of the pregnancy, provided the patient's general condition permits of it.
4. The examination of the fundus of the eye of the patient suffering from vomiting in pregnancy is as important as in the toxemias occurring later in gestation.
5. The occurrence of retinal hemorrhages should indicate further clinical study, especially of the genitourinary tract.

I wish to acknowledge indebtedness to Dr. Benjamin P. Watson, director of the Department of Obstetrics and Gynecology of the Sloane Hospital for Women and to Dr. William C. von Glahn, Department of Pathology, Presbyterian Hospital.

While the article was in press, another case was encountered in which retinal hemorrhages appeared two days following termination. The patient has survived, although a bilateral flaccid paralysis of the lower extremities and a Korsakoff syndrome are present.

SUBACUTE BACTERIAL ENDOCARDITIS IN PREGNANCY

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SUBACUTE bacterial endocarditis as a clinical entity was described by Osler as early as the year of 1852. Since that time, many cases have been reported but, of these, surprisingly few have been associated with pregnancy. The early writers were mainly interested in the predisposing factors of the disease, and were divided into two groups: the one believing rheumatic fever to be an underlying factor, the second group adhering to the theory of previous damage done to the heart valves of patients later suffering from endocarditis. Some of these authors suggested that the predisposing damage could have been effected by the same organism as the one causing the terminal disease. How soon such effects could be seen clinically would depend upon the severity and duration of the infection, the frequency of the attacks, and the freedom from symptoms between the attacks. This idea of a free interval phase has grown to be a well-recognized clinical aspect of the disease and has been described by Libman in his recent work as the "bacteria-free stage." During this period the patient may be quite free from any signs or symptoms except for the damage already done to the valves of the heart. During an exacerbation of such an attack, all the cardiac findings are exaggerated, and to them are added a second group caused by the invading organism. This is shown clinically as a generalized septicemia.

Crom described a case associated with a pregnancy of eight months' duration, where the temperature, profuse perspiration, rapid pulse, and fatigue dominated the picture, while Burgess cites a case in a woman, six months' pregnant, with no previous cardiac history prior to the onset of the endocarditis, from which the patient died of cardiac failure. Blumer, although primarily interested in the cardiac damage done in subacute bacterial endocarditis, also describes the extracardiac or toxic group of symptoms. Most writers agree that the invading organism in most cases injures the mitral valves of the heart, doing very little damage to the myocardium. As a result, the cardiac symptoms are usually of a mechanical nature, the patient usually showing very little if any myocardial failure.

The second group of symptoms are extracardiac, embolic in nature, thus accounting for the petechiae, the Janeway lesions, and the embolism into the spleen, brain, and kidney. Since these emboli are infected when lodged in the kidney, they will, according to MacCallum, account for the glomerulonephritis often associated with and mistaken for the disease. The fever, rapid pulse, pallor, and increasing anemia may be accounted for by the bacteriemia.

Five cases of subacute bacterial endocarditis associated with pregnancy are reported in the literature by Walser (2), Kobacker (1), and Mengert (2). These

cases all showed mitral lesions except the one of Kobacker, which showed a mitral lesion as well as involvement of the aortic valve. Two of these 5 patients and the one from the New York Hospital gave a history of a persistent unproductive cough, an interesting feature explained by Pardee as due to lymph drainage of the cardiac lesion into the tracheal lymph nodes. The pressure of these lymph nodes caused a constant irritation which, in turn, would explain the cough.

The age incidence in these 5 patients reported in the literature ranged from eighteen to twenty-seven years. Multiparity varied, 3 being primigravidae, 2 having had one pregnancy each, and one having had 5 pregnancies. The onset of the illness was from the third to the ninth lunar month of gravidity. The onset of the disease was always insidious and accompanied by weakness, loss of weight, fever, rapid pulse, and marked pallor. The hemoglobin content of the blood ranged from 35 to 50 per cent and polymorphonucleosis was always present. The examination of the urine always showed an albuminuria with gross and microscopic blood present. The duration of labor was approximately seven hours and was terminated by spontaneous vertex delivery in 2, breech extraction in 2, and low forceps delivery in one patient. One cesarean section was done to save the baby after hope for the mother was given up; the baby lived and the mother died four days postpartum. The infants ranged from 1,770 gm. to 2,558 gm., all born alive but one dying twenty-seven hours after delivery. The second maternal death occurred thirty-two days postpartum, the third fifty-one days postpartum, and the fourth six months postpartum.

One interesting feature is the fact that the patient, who became rapidly worse and was delivered by section as a choice to relieve the strain of labor, gave a past history of two attacks of rheumatic fever during childhood. Furthermore, the patient who died on the thirty-second day postpartum suffered from rheumatic fever in childhood and repeated sore throats, until a tonsillectomy in 1922, death of the patient occurring in 1928. In the third fatal case, ending on the fifty-first day postpartum, the patient had a history of measles, parotitis, and tonsillitis in childhood and died at the age of twenty-seven years. The patient who lived six months suffered from scarlet fever and pneumonia in childhood.

The history record of the patient from the Woman's Clinic of the New York Hospital is as follows:

A white female, unregistered, para 1, aged twenty-one years, was admitted to the hospital March 2, 1933, in the ninth lunar month of pregnancy. Her last menstrual period was in June, 1932.

Past History.—There was no history of rheumatic fever, scarlet fever, tonsillitis, mumps, measles, or influenza. In 1931 she had a normal spontaneous delivery of a normal, 3,300 gm. baby, duration of labor being thirty-six hours.

Present Illness.—The history of her present illness dates back to three months prior to admission. At that time she tired easily, was weak, and found it an effort to carry out her domestic duties. In February she had chills and fever, and remained in bed six days. Ten days prior to admission the patient had a sharp pain in her right side, just above her hip. On admission she complained of pain in the right half of her chest. The pain was sharp in character and radiated posteriorly. The past two weeks prior to admission, the patient complained of an unproductive cough and one week later noticed that her ankles were beginning to swell.

Examination on Admission.—Examination showed a well-nourished white woman, skin dry, temperature 39.2° C. (102.4° F.), pulse 124 per minute, respirations 24. There were petechiae on the right lower lid and the nail bed of the little finger of the left hand. Examination of the throat revealed nothing abnormal, and the thyroid was not enlarged.

Examination of the chest gave dull percussion notes at both bases, with many medium, moist râles, more numerous on the right side.

The heart borders extended to 6 cm. on the left and 3 cm. on the right side. A systolic thrill was palpable at the apex. There was a harsh presystolic murmur at the apex followed by a blowing murmur. Over the base a blowing systolic murmur was heard. Her blood pressure was 130/90.

The abdomen was not tender and showed no rigidity; the liver and spleen were not palpable. The uterus was symmetrically enlarged to the size of an eight months' pregnancy, the fetus presenting by the vertex, the fetal heart being heard in the left lower quadrant at a rate of 154 per minute.

Examination of the extremities did not show edema.

Antepartum Course.—Her daily temperature ranged from 35° C. (95° F.) to 40° C. (104° F.), with the highest average point during the twenty-four hours occurring at 8:00 P.M.

March 3 to March 9, 1933: General condition remained unchanged.

The following investigations were carried out. A blood culture, taken March 3, 1933, grew *Streptococci viridans*, 200 colonies per cubic centimeter. A catheterized urine specimen on the same day was positive for *Staphylococcus albus*.

A blood chemistry report on March 3, 1933, gave normal values. A phenol-sulphonephthalein kidney function test showed delayed and poor excretion.

A blood culture taken on March 5, 1933, grew *Streptococcus viridans*, 300 colonies per cubic centimeter.

X-ray pictures of the chest and abdomen showed (1) heart enlarged, triangular in shape; (2) fetus in uterus, approximately eight months.

Labor.—The patient went into labor spontaneously on March 9, the seventh day after admission. The duration of labor was four hours and forty-five minutes. Ether was administered by open drop method, and the patient was delivered by low forceps, the indication being maternal distress. The perineum was intact, and the placenta was expressed from the vagina. The amount of blood loss was 300 c.c. The child was a normal male, weighing 2,310 gm., and having a biparietal measurement of 8.5 cm.

Examination of the placenta and membranes showed the latter to be unusually friable. The weight of the placenta and membranes was 370 gm. Sections of the placenta were made and these appeared normal under the microscope. The placenta was stained to demonstrate organisms, but none were found.

Postpartum Course.—Following delivery the patient's condition showed no change.

A culture taken by swab from the blood on the cervix at the time of delivery was reported to be positive for *Streptococcus viridans*, anaerobic staphylococcus, and diphtheroids. A catheterized urine specimen at the time of delivery was positive for *Streptococcus viridans*. A culture from the cord blood and placenta showed no growth after five days. A blood culture from the baby at the time of delivery grew hemolytic staphylococcus aureus in plain broth, but showed no growth in dextrose or blood agar plates after twelve days.

A second blood culture was taken two days after delivery and was negative.

A uterine culture from the patient four days postpartum was positive for *B. coli*, *B. welchii*, anaerobic nonhemolytic streptococcus and aerobic nonhemolytic streptococcus, which did not cause greening on agar.

A blood culture eight days postpartum grew *Streptococcus viridans*, 200 colonies per cubic centimeter.

On the eleventh day, the patient was transferred to Medicine.

A summary of the blood study during her entire stay in the hospital showed repeated tests for hemoglobin which ranged from 60 per cent (first examination)

to 33 per cent (last examination). The number of red blood cells ranged from 3,000,000 on admission to 1,920,000 on the last examination. The white blood count averaged 10,360. The examination of the urine in 15 specimens (two catheterized, others voided) showed repeated albuminuria, hematuria, and white blood cells, while microscopic examination showed occasional cellular casts, few hyaline casts, and many granular casts.

Treatment.—The patient was given general palliative treatment. Digitalis was used in doses of 0.10 gm., repeated three times a day. Morphia was used for rest when needed.

The baby was taken off the breast and transferred to the premature nursery, and was discharged from the hospital on the twenty-eighth day, weighing 2,820 gm., 510 gm. above its birth weight.

Follow-Up Notes.—The baby was readmitted to the hospital on April 13, 1933, with a temperature of 38.2°, vomiting, and diarrhea. The baby would not take its feeding. Its weight on admission was 2,520 gm. On April 21, 1933, its temperature had been normal since the day of admission, and it had no diarrhea, no vomiting, and was taking its feedings well, weighing 2,630 gm. Examination of the child at this time was apparently normal. The diagnosis on the baby, during this admission, was gastrointestinal intoxication.

The mother was visited in her home by the Social Worker who was told that the patient had improved slightly since she left the hospital.

SUMMARY

In reviewing the above case history, one is impressed by the fact that the culture from the cervix was reported positive for *Streptococcus viridans*. The cervix was bleeding, the swab contained mostly blood, so that this was really a blood culture. The uterine culture, taken four days postpartum, showed aerobic nonhemolytic streptococcus, but this did not cause greening blood agar plates and was not *Streptococcus viridans*. Moreover, the cord blood and placental blood were both negative. Following delivery, there was never any exacerbation of symptoms, and a blood culture eight days postpartum showed 200 colonies of *Streptococcus viridans* per cubic centimeter. Such findings strongly suggest that the bacteriology in subacute bacterial endocarditis is quite different from the organisms that usually inhabit the pelvic organs. This is also borne out by the clinical course of this patient.

DISCUSSION

Of the 5 patients referred to previously, 4 died. Autopsies were performed on 3, while the fourth patient died at home, six months after being discharged from the hospital. In 2 of the 3 postmortem examinations, there appeared scarring and damage to the mitral valves, the third patient showed this in addition to scarring and thickening on the aortic valve. Of the 3 patients dying in the hospital, cultures were taken from the mitral valves of two patients and were positive for *Streptococcus viridans*. The blood cultures taken on the above four patients varied from 2 to 7 in number, in each case, and were positive for *Streptococcus viridans* in all, except the first two taken before de-

livery on one patient of the Mengert. Cultures on the cord blood and in the infant were not taken on 2 of the above fatal cases, but the cultures on the cord blood in the other cases were positive on two occasions. In both babies the blood cultures were negative two weeks after the positive cord cultures were obtained.

The only fetal death was the infant weighing 1,700 gm. This is not an unusual termination for a baby so premature. An autopsy done in this case showed multiple infarcts in the brain. Blood cultures taken from the spleen of the child were negative, while a blood culture taken from the heart was positive for *Streptococcus viridans*.

In each of the preceding 6 cases just reviewed, one finds that the onset of the terminal illness was not related directly to the duration of pregnancy. It depended more upon the past health of the patient. The most severe cases took place in persons with a history of previous cardiac disease, especially that of rheumatic fever.

The organism invading the blood stream in cases of subacute bacterial endocarditis during pregnancy was the *Streptococcus viridans*. This organism is not frequently found in the pelvic organs. Clinically the cases were not aggravated by labor, and therefore, one would be inclined to allow pregnancy to progress to term whenever possible.

The management of labor in patients with subacute bacterial endocarditis should be governed by the condition of each case as it presents itself. The patients delivered by conservative methods did better than those treated more actively.

The maternal death rate was high, as one would expect from the death rate in this disease in nonpregnant patients. The only fetal death occurred in a premature infant. The babies apparently escape the infection during their intrauterine life. The follow-up reports on the infants showed them all to be doing well. The period of follow-up on these children was only six months. It may, therefore, be interesting and instructive to follow up these children over a much longer period in order to determine whether or not they are more prone to develop cardiac disease as they approach maturity.

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CALCIUM IN THE TREATMENT OF DYSMENORRHEA

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AND

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A GROUP of symptoms occurring in pregnant women has been described¹ and the explanation for their presence presented as being apparently due to a deficiency in calcium. In a later paper² the relation of this group of symptoms with other factors, particularly dysmenorrhea, was described. A definite correlation between the symptoms and dysmenorrhea was found. It seemed likely that the indirect relationship thus shown between dysmenorrhea and calcium deficiency might be direct and definite.

A limited investigation of this possibility was therefore undertaken at the Students' Health Service of the University of Minnesota upon a group of undergraduates, each of whom had menstrual cramps severe enough to incapacitate her for one or more days each month. All of the patients were unmarried women, the mean age of the group being 20.3 years. Menstrual histories revealed no cases of menorrhagia, metrorrhagia, or oligomenorrhea.

Forty-nine cases of dysmenorrhea were treated. The therapy consisted of calcium gluconate alone, calcium gluconate with viosterol, alkaline mixture alone, or calcium gluconate and the alkaline mixture. Pelvic examinations were made on about one-half of the patients.

Of the 49 patients treated, 33 had either complete relief from abdominal pain, leg cramps, paresthesias, and nausea, or felt that they were definitely benefited, while 16 had no improvement.

Table I shows the type of therapy used and the findings at the pelvic examination in the two groups, those benefited by the therapy and those receiving no benefit.

The calcium was administered in the form of calcium gluconate by mouth. Sixty grains of calcium gluconate were given daily for ten to fourteen days before the onset of the menstrual period and continued through the first two days of the period. When viosterol was given with the calcium gluconate the dosage was thirty drops daily during the same period.

The alkaline mixture, which was used alone in a few cases and with calcium gluconate in other cases, consisted of equal parts of magnesium carbonate and sodium bicarbonate. The dosage used was

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sixty grains three times a day for ten days before the onset of the menses. This alkaline mixture was tried because it had come to our attention that in one of the Teachers' Colleges in this state, the school

TABLE I

MEDICATION	NO. CASES	PELVIC EXAMINATION	NO. CASES
<i>Cases Benefited by Calcium Therapy</i>			
Calcium Gluconate	9	Negative	5
Calcium Gluconate and Viosterol	16	Retroversion	3
Alkaline Mixture	5	Anteflexion	6
Calcium Gluconate and Alkaline Mixture	3	Cystic ovary	2
	—	Not done	17
Total	33		—
		Total	33
<i>Cases Not Benefited by Calcium Therapy</i>			
Calcium Gluconate	5	Retroversion	5
Calcium Gluconate and Viosterol	9	Anteflexion	1
Alkaline Mixture	2	Not done	10
	—		—
Total	16	Total	16

nurse, who suffered from severe dysmenorrhea happened to take an alkaline mixture, of similar composition, for a gastrointestinal upset that coincided with her menstrual period. To her surprise, this menstrual period was painless. The following period she repeated the medication and again was free from pain. She then gave this alkaline mixture to some of the students who had severe dysmenorrhea with equally good results. What the effect of magnesium carbonate in preventing dysmenorrhea may be is unknown. Carswell and Winter³ have shown that with adequate phosphorus intake, magnesium appears to favor calcium storage instead of causing calcium loss.

There seems to be little therapeutic difference with variations of the drugs. The alkaline mixture was used less frequently than the calcium and viosterol, however.

In all of the cases reported, the drug was taken before two or more menstrual periods.

Each case in this series is considered to be one of essential dysmenorrhea in the sense that in no instance, so far as could be determined, was it an "aggravation during the menstrual congestion of the more or less continued pain from various pelvic disorders, such as salpingitis, pelvic inflammation, appendicitis, chocolate cysts, etc."⁴

Since all cases were apparently alike in being of the essential type, some factor in the symptoms was sought which might indicate a significant difference between those patients who were relieved by calcium and those who were not. With one possible exception, none was found, so that the distinction between the two groups remains largely a therapeutic one.

TABLE II. PERCENTAGE OF CASES HAVING CERTAIN SYMPTOMS

	BACKACHE		BRUISE EASILY		LEG CRAMPS		NAUSEA		TENSE TYPE	
	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT	NO.	PER CENT
Cases Improved	19	57.5 ± 6.3	13	68.4 ± 7.1	13	54.1 ± 6.7	13	54.1 ± 6.7	16	53.1 ± 6.1
Cases Not Improved	9	56.2 ± 6.3	2	18.1 ± 7.8	5	38.4 ± 9.1	9	75.0 ± 8.4	9	64.2 ± 8.6
Differences in Percentages		1.3 ± 8.85		50.3 ± 10.55		15.7 ± 11.3		20.9 ± 10.77		10.9 ± 10.54

NOTE: In tabulating the data, some of the items were rejected from consideration for various reasons. In each case percentages were derived for the number of items remaining under each group after elimination of rejected items.

It is apparent that the symptom of bruising easily is a significant one, so much so that its mathematical exposition was expected from the regularity with which it appeared clinically. Fifty per cent more of the cases which were benefited by this therapy gave a history of bruising easily than of the cases receiving no benefit from calcium. Since this difference in percentage is five times the probable error of the difference, it is of definite statistical significance.

The basis for this symptom perhaps lies in the effect of calcium upon capillary and vessel permeability. Cantarow⁵ refers to this question in his work on calcium. Loeb⁶ states that a certain concentration of calcium ions tends to make capillaries impermeable and to constrict vessels, while potassium ions, if not counteracted by calcium, tend to have an opposite effect. Spiegler⁷ has shown that while there is but little variation during the menstrual cycle of the blood calcium, there is quite an appreciable variation in the potassium content of the blood, rising just before menstruation, decreasing during the flow, and later regaining the normal level. It has also been pointed out⁸ that the serum calcium level in women having dysmenorrhea shows no demonstrable difference from that of women having no menstrual pain. In a personal letter to one of us (R. E. B.) Burnett⁹ has suggested that this disturbed calcium-potassium ratio may be of importance in that it might explain certain beneficial effects of calcium therapy, even though there existed no apparent diminution in calcium levels. Whether there is a connection between this factor of easy bruising and the coagulability of blood is not known. Hunter¹⁰ states that there is no evidence to indicate a calcium defect in hemophilia.

The production of pain in the menstrual process appears to be due to an increased irritability of the muscles and nerves involved, smooth muscle and the autonomic nerves being affected equally with the other parts of the nerve and muscle systems. The rôle of calcium here is, as Hunter says, to maintain, along with the other ions, a balanced system determining the degree of irritability of muscle and nerve. "In this way calcium ions help to control the heartbeat, and contractility of plain and striped muscle, and the transference of impulses at the neuromuscular junctions and through synapses. In general, it may be stated that calcium ions play an important part in lessening the irritability of the tissues containing them."

SUMMARY

Of 49 cases of essential dysmenorrhea treated with calcium, or calcium and viosterol, 33 or 67.3 per cent were greatly benefited; 16 or 32.7 per cent seemed to have no relief.

The symptom of bruising easily seems to indicate, in cases of essential dysmenorrhea, that a more favorable response to calcium therapy may be expected than in cases without this symptom.

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MALIGNANT NEOPLASMS OF THE OVARY

AN ANALYSIS OF ONE HUNDRED AND FIFTY CASES

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THE usual results following surgery in the treatment of malignancy of the ovary have not been very encouraging. Though occasionally a patient so treated may live for a period of five or six years, in most cases, the average duration is only two years.

In January, 1932, the author reported a case of malignant disease of the ovaries with recurrence and metastases, treated by surgery and radiation,¹ still under observation thirteen years after treatment, and the patient is in apparent comfort, attending to her daily duties as secretary. This cooperation between the surgeon and radiation therapist offers the best results obtainable in the care of these difficult cases.

During the period of eight years from 1924 to 1931, inclusive, 150 patients with malignant diseases of the ovaries were admitted to the hospital and clinic division of the New York City Cancer Institute. The majority of these patients had already been treated elsewhere and were in, more or less, hopeless condition; and in many, complete data were unobtainable regarding their previous condition and treatment. Such information on hand, however, has been used for the conclusions herein expressed, regarding the therapeutic measures best suited for this condition.

The youngest was eleven, the oldest was seventy-four. The three patients under twenty were eleven, sixteen, and seventeen years of age, respectively. Most of the patients, or 78 per cent, were between the ages of thirty-one and sixty. About 80

AGE INCIDENCE OF MALIGNANT DISEASE OF THE OVARY

AGE	NUMBER OF CASES	PER CENT
Under 20 years	3	2
21 to 30	5	6
31 to 40	31	20
41 to 50	57	36
51 to 60	33	22
61 to 70	15	10
71 to 80	6	4

per cent of the women were white and 20 per cent colored. Approximately 60 per cent were among Jewish women. There were 120, or 80 per cent, married and 30, or 20 per cent, unmarried. Seventy-five, or 50 per cent, had borne no children. The other 50 per cent had from one to thirteen children. About 15, or 10 per cent, had a history of one or more miscarriages, and one had a twin pregnancy.

The most common symptoms were pains in the abdomen, swelling, or increase in size, and mass in the abdomen, with loss of weight and strength. The character of the pain varied from a soreness, or sense of pressure, dull, or cramplike, to sticking in nature. The location of the pain varied from epigastric to lower abdomen, in the suprapubic, or left or right lower quadrants of the abdomen, to the lower lumbar region. Pain was present in about 80 per cent of the cases; most frequently in the lower abdomen and next in the lower lumbar region.

Swelling, or increase in size of the abdomen, was present in about 50 per cent of the cases. A mass in the abdomen, varying from a single, hard, nodular to multiple masses, occurred in about 40 per cent of the cases. Loss of weight and strength was noticed in about 35 per cent of the series.

About 30 per cent of the series gave a history of menorrhagia, metrorrhagia, dysmenorrhea, amenorrhea, or irregular vaginal bleeding; in 75 per cent of which the amount of flow was increased; in 15 per cent dysmenorrhea, and in 10 per cent amenorrhea.

Ascites was present in about 50 per cent of the cases, varying from yellow, straw-colored, serosanguineous to bloody in color. Presence of tumor cells was reported in two instances.

Constipation, dyspnea, vaginal discharge, urinary disturbances as dysuria and urgency, faintness and dizziness, edema of the lower extremities, jaundice are among the other less frequent symptoms. Among the other less common clinical findings present were pleural effusion, most often unilateral and on the left side, hard metastatic glands most frequently inguinal, but also supraclavicular and in axilla. Abdominal fistula were present in two cases; and in one, a vesico- and rectovaginal fistula. In one case there was roentgen evidence of a lesion in the pylorus with metastases in the lung (Kruckenberg tumor) and in another roentgen evidence of a pathologic fracture in the right hip, due to metastases in the ischium and femur. Operation for intestinal obstruction was done in one case and the findings showed the obstruction to be due to malignancy of the ovaries.

In three cases there were histories of other previous primary tumors, which had been treated before. These lesions were carcinoma of breast, epidermoid carcinoma of the skin of the forehead, and squamous cell epithelioma of the left antrum.

The duration of symptoms from onset until diagnosis was made, varied from a minimum of one month to as long as three years, with an average of nine months.

The duration of symptoms was within one year in 85 per cent of the series. The shortest from time of diagnosis to treatment by surgery, was one month, and

TOTAL DURATION FROM ONSET TO EXITUS WITH OPERATION
NUMBER OF CASES 71. SHORTEST, THREE MONTHS. LONGEST, SIX YEARS (1 CASE)

DURATION	NUMBER OF CASES	PER CENT
Three to 6 years (average 4)	12	15
Less than 3 years (average 19 months)	31	45
Less than 1 year (average 7 months)	28	40
Total duration, of less than three years, about 85 per cent.		
Average duration of the whole series was 19 months.		

the longest was thirty-two months; the average being twelve months. About 70 per cent of the patients were submitted to operation. Radiation therapy was instituted in about 12.5 per cent of the patients.

TOTAL DURATION FROM ONSET TO EXITUS, WITHOUT THERAPY

Number of cases	35	{ Minimum, 1 month
		{ Maximum, 6 years
Average		16 months
Duration less than 1 year		60 per cent
Duration 1 to 2 years		25 per cent
Duration 3 to 6 years		15 per cent

There were 15 patients under observation, which were treated by surgery and radiation, most of which were under observation from one and one-half to three years, with one patient still under observation for a period of six years.

PATHOLOGIC FINDINGS

Adenocarcinoma	38
Papillary cyst adenocarcinoma	27
Teratoid embryonal carcinoma	7
Metastases in liver	4
Metastases in lung	4
Metastatic papillary adenocarcinoma in cervix	4
Adenocarcinoma in stomach and ovary, with metastases in lung (Krukenberg)	4
Colloid carcinoma	1
Malignant papilloma	1
Alveolar sarcoma	1
Papillary cyst	1
Chondromyxosarcoma	1
Metastatic adenocarcinoma of abdominal wall	1

Autopsy was performed in 9 and the findings were as follows:

1. Recurrent adenocarcinoma of the ovary with metastases to the urinary bladder, liver, peritoneum, mesenteric and retroperitoneal glands, supra- and infra-clavicular glands, diaphragm and both iliopsoas muscles.
2. Adenocarcinoma of the ovaries with metastases to the mesentery, liver, spleen, peritoneum, diaphragm, lesser curvature of the stomach, pericardium, right supra-clavicular glands.
3. Papillary adenocarcinoma of the ovaries with metastases in the mesentery, liver, and peritoneum.
4. Adenocarcinoma of the ovary with metastases to the peritoneum, stomach, intestines, right dome of diaphragm.
5. Adenocarcinoma of the ovary with invasion of the uterus.
6. Adenocarcinoma of the ovary with invasion of the uterus.
7. Annular carcinoma of the pylorus of the stomach with metastases to the ovaries and peritoneum.
8. Adenocarcinoma of both ovaries with extension of the parametrium and cervix; metastases in the omentum, peritoneum, liver, diaphragm, capsule of the spleen and lung.
9. Papillary carcinoma of the ovary with metastases in the omentum, liver, pleura and pelvic glands, and peritoneum.

CONCLUSIONS

The diagnosis of fibroid uterus proving to be a malignancy of the ovaries at operation is not uncommon. A history of pains in the abdomen, increase in size, with some loss in weight and strength, with perhaps some irregularity of menstrual function, should bring to mind the possibility of malignant disease of the ovaries.

The management of these cases is very difficult and from the study of this series, it seems that surgical measures alone do not show very encouraging results. Radiation therapy has only been used in a small percentage of this series and it would be unfair to draw any conclusions therefrom, especially for the reason that the majority of the patients were, more or less, beyond any form of specific therapy.

In patients in whom malignant disease of the ovary is suspected, it might be a good procedure to administer a course of radiation therapy before operation and possibly convert an inoperable condition into one of operability, to be followed by postoperative radiation therapy.

It is possible that by early cooperation between surgeon and radiation therapist in the management of such patients, better and more encouraging results will be obtained in the future.

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40 WEST SEVENTY-SECOND STREET

MISSED ABORTION WITH SUPERIMPOSED PREGNANCY*

A CASE OF COMPOUND INTRAUTERINE GESTATION

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THE occurrence of missed abortion is not a rarity. However, the fact has not been recorded that a superimposed pregnancy carried to term may follow in the course of a missed abortion, as revealed in a careful review of the literature available, and in an exhaustive study of the references obtainable.

Simpson,¹ in considering the terms, implied "compound pregnancy" to include all varieties of extra- and intrauterine pregnancy, while Novak² feels that the term should only apply to cases of pregnancy which occur during the presence of remnants of a prior gestation, such as extrauterine fibrotic or hyalinized villi or lithopedion formation; leaving the term "combined pregnancy" to apply to those instances in

which the extra- and intrauterine pregnancies are of approximately the same age. As Weintraub³ and others have pointed out, combined pregnancy is essentially a twin pregnancy in which one ovum lodges in the uterine cavity, and the other remains ectopic.

Accepting Novak's viewpoint, we find the literature replete with instances of unusual interest from the standpoint of compound pregnancies.⁴⁻¹² But in none of them was the phenomenon manifested by concomitant intrauterine gestations. All of the ensuing intrauterine pregnancies occurred in the presence of extrauterine fetal remnants.

It is evident, of course, that the factors obtaining in a presumptive case of superfetation are not entirely the same as those affecting a case of missed abortion with superimposed pregnancy. Here the dead fetus represents a foreign body. The cervical mucous plug can be disregarded as can the closure of the oviducts. The ability of the sperm to traverse the uterus should be no more hindered than in an instance of a large fibroid or other tumor mass. With the death of the fetus we should not expect the corpus luteum to offer a further resistance to ovulation, even if this were so in all cases. And likewise with the death of the fetus, and further ovulation, a decidual reaction would be expected for the supervening pregnancy.

Consequently the possibility of the occurrence of such an anomaly as a superimposed pregnancy in a case of missed abortion cannot be denied from a consideration of the factors involved in the ordinary case of pregnancy.

We must, of course, recognize that the liability of abortion or miscarriage would be greatly increased, nevertheless this liability does not prevent entirely the possibility of such an event progressing to term, as is presented in the case report to follow.

In our review of the literature, the only case report we have found which appears similar in some respects and which might be considered a superimposition of pregnancy in a missed abortion is that of Carpenter,¹³ who titles the report as "a case of miscarriage with two distinct ova of different ages." In the description of the patient, a young woman of twenty-four years was in fair health until the tenth week when she expelled an ovum which proved to be about the age of three weeks. The presence of a second ovum was considered possible; later a fleshy mole was passed of the usual ovoid shape and about four inches in diameter. In a discussion of this case Dr. G. S. Mitchell says, "Is it not probable that, as soon as the product of the first conception became a 'mola carnea' it lost its power of inhibiting the ovarian function, and was virtually a foreign body in the uterine cavity when the second impregnation supervened? This would explain satisfactorily the second fecundation and also the abortion." The case report, however, is indefinite in many aspects, and other discussants tend to cast considerable doubt on the case as to the true nature of the probable conditions obtaining, leaving the matter largely to inference. Moreover it differs decidedly in that the case did not progress to term.

The case to be presented does not in any way affect the status of the question of possibility of superfetation, superimpregnation, superfecun-

dation, or the occurrence of a papyraceous twin, but the interpretation of the facts does indicate that in the presence of a missed abortion, pregnancy may supervene and go on to term.

Mrs. I. S., housewife, white, aged twenty-eight, para ii, entered St. Margaret's Hospital June 22, 1928, at full term. She was brought to the hospital before the onset of labor, because of the peculiar course of her pregnancy, and for the purpose of inducing labor. The indications for this procedure are brought out in the history of the case which follows:

In 1922 she had been delivered of a full-term child, by a forceps delivery, the child dying either during or shortly after delivery, and the cause was unknown. Since September of 1924 she had been seen at varying intervals for minor complaints, and in February, 1926, she had been curetted elsewhere for a menorrhagia of several weeks' standing, for which a self-induced abortion was suspected as the cause, but which the patient would not admit. No report as to the examination of curettings.

On June 13, 1927, the patient was first seen because of the question in her mind of a possible pregnancy. Last normal menstrual period April 16, 1927. No previous irregularities, except normal interruption in 1922, and profuse flow in 1926. No other subjective symptoms of possible pregnancy except increased frequency of urination.

Examination at this time gave the following essential findings:

Breasts were large and pendulous. Few linea albicantes or striae gravidarum were present. Nipples were dark and puffy. No colostrum was expressed. Primary areola was dark and well defined, and no secondary areola was present.

Vaginal examination showed a positive Chadwick, and Hegar's sign. Uterus was soft in consistency, enlarged and rounded.

In view of these findings and the history of the absent menses, the patient was told that she was probably pregnant. Measurements all within normal limits. Blood pressure, general physical examination, and urinalysis were all normal. Blood Wassermann was negative. Date of expectancy was Jan. 23, 1928.

Regular monthly visits showed normal findings, and satisfactory progress. Uterus was palpated in the suprapubic region. Aug. 30, 1927, fundus was near umbilicus, continued satisfactory progress. Next visit was October 10. At this time she stated that on September 15 she had had some bleeding for one day, but had not flowed since. The reason for this flow of blood was not divulged until about three months after the final termination of her case, when it was brought out that in the middle of September she had been struck in the abdomen by a baseball, and shortly after had noticed the flow of blood. Examination disclosed the uterus to be smaller than on previous visit. Abdomen was obese. No fetal movements were felt. Question of hydatid mole was considered, but there were no irregular hemorrhages. Missed abortion seemed likely, and in absence of symptoms patient was advised to return in one month.

November 24, uterus was slightly larger than at previous examination. It was palpable as an indefinite soft mass about 2 cm. below the umbilicus. There were no fetal movements, no bleeding, no pains. Diagnosis was shrouded, and conservative waiting pursued.

In January, 1928, uterus was found to be still larger. Patient was referred to Dr. Arthur Curtis for consultation. His diagnosis was that of "missed abortion," with request that patient be returned in one month for further examination, provided she remained free from symptoms.

In February, 1928, she refused further consultation. Uterus progressively enlarging. X-ray examination showed a large blurry mass, but no fetal parts were made out. Findings were distinctly opposite from those expected in a missed abortion, and consideration of this was dismissed. Uterus was enlarging, and there were no pains, no bloody show, no toxic symptoms. An Aschheim-Zondek test would have been of considerable value at this time.

Original date of expectancy was passed. Uterus was above the umbilicus. General physical condition continued good. Early in March the patient advised that she had been feeling life for two weeks. Examination disclosed continued enlargement of uterus. Diagnosis of definite pregnancy probably complicated by abnormal growth of uterus which had simulated pregnancy previously. New date of expectancy, based on flow of blood in September, 1927, computed for June 22, 1928.

Beyond unusual enlargement, further progress was uneventful. Twin pregnancy was not suggested from findings. Fetal parts were made out and one set of heart tones was audible.

June 10, 1928, head found fixed in the pelvis. Correctness of expectancy date appeared definite. June 22, patient was sent to hospital for induction of labor. Membranes were stripped, and divided doses of quinine followed by castor oil were given. Few slight weak contractions in response. Procedure was repeated the following day, and three minims of pituitrin were given in addition. Reaction was better, but pains were weak, of short duration, and productive of little progress. Membranes ruptured spontaneously in the evening, and pains recurred about every minute accompanied by some bearing down sensations. Flow of amniotic fluid was excessive, but practically no progress was made in delivery. On the morning of the third day pains stopped entirely. There was no advancement of the head, and very little dilatation of the cervix. The possibility of a tumor obstructing and retarding the course and progress of her labor appeared very likely.

We were aware of the notorious indolence of the uterus in cases of missed abortion, and DeLee's¹⁴ statement that after days of failure in getting regular pains started, he has had to resort to operative measures. But we were not entirely convinced that a missed abortion had existed. We felt that the peculiar course of pregnancy first of all was sufficient to indicate that there was something entirely wrong, and that we could at least expect some difficulty even if the patient had gone into normal labor. We further felt that the patient was at full term, and we knew that the fetus was alive. We further had attempted to give her a test of labor by inducing it, and had found the uterus atonic, and with practically no expulsive power. We therefore felt that further measures along this line, such as the use of a bag, would be of little avail. While the patient had had one clean vaginal examination, we did not care to subject the uterus to any further danger of infection in case we finally had to do a cesarean section. The circumstances were explained to the patient and her consent secured to do a cesarean section, together with a hysterectomy in case the findings warranted this procedure.

The classical section was done, and a normal full-term male child, weighing 6 pounds and 14 ounces, was delivered. In the delivery it was necessary to go through the placenta which was attached to the anterior uterine wall. The membranes were delivered with the placenta, and were found to compose the single unit for the child just delivered. We then found a smaller intact sac of a dark greenish color, which was opened and drained of a greenish brown fluid. Within the sac a dead, partly macerated female fetus was found, corresponding in size and development to that of about five months. The sex was easily determined, and the fetus measured 18 cm. in length. Besides being slightly macerated, it showed the usual evidence of compression, in that the head was flattened and the anteroposterior diameter of the body narrowed. It resembled the condition found in the fetus of twin pregnancy

which dies early and becomes compressed against the wall of the uterus through the development of the living fetus, the so-called papyraceous or compressus. However, we are certain that this was not the situation in this case because of the history and course of the pregnancy. The uterus, tubes, and ovaries were entirely normal. A separate placenta attached to the posterior wall of the uterus was delivered, and found to be flattened, dark, and somewhat necrotic, with the cotyledons practically obliterated. No tumor masses were found. The uterus was not of the bicornuate or arcuate type, and there was no septum dividing it into separate cavities.

Comment.—The conclusions reached in this case are, that the patient undoubtedly became pregnant in April, 1927, and the course of her pregnancy up until September was normal. When she was struck in the abdomen by the indoor baseball, the fetus present in the uterus died, and the diagnosis of missed abortion was correct. However, before another month had passed she became pregnant again, and she admits the intercourse at this time which was responsible. She then continued to carry both a living and a dead fetus for nine months, until delivered by cesarean section, the dead fetus having been carried in utero for fourteen months, five months as a living fetus and nine months as a dead one. The second or superimposed pregnancy pursued a normal nine months' gestation period.

Convalescence was uneventful and a rapid recovery was made. The child is well and has developed normally. The mother has since had her gallbladder removed for cholelithiasis, and has just recently delivered spontaneously a living female child, following a normal gestational period.

A review of available literature has not revealed a case report of missed abortion with superimposed pregnancy going to term, and the case here presented of such a compound intrauterine gestation is submitted as an instance revealing the possibility of its occurrence. It is not confused with the questionable occurrence of superfetation, superfecundation or superimpregnation, as each supposes the existence of a previous live fertilized ovum. Neither is it confused with the occurrence of a twin pregnancy with fetus papyraceous, as a consideration of the facts obtaining indicate. Any consideration of a uterus didelphys, bicornuate or arcuate uterus is ruled out because of the findings at the time of section.

We feel that the use of an Aschheim-Zondek or modification of this test should prove of great value as an aid in situations of this kind, although admittedly it might only serve as a check upon an otherwise radical procedure.

From a consideration of the facts presented and an interpretation of the sequence of events, the possibility of the occurrence of missed abortion and superimposed pregnancy, or more properly perhaps, of compound intrauterine gestation is advanced.

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137 RIMBACK AVENUE

THE INDUCTION OF LABOR BY RUPTURE OF THE MEMBRANES

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RUPTURE of the bag of waters was probably the first method ever employed for the induction of premature labor. It was certainly used in England as early as the Eighteenth Century.¹ During recent years the method has regained some of its former popularity. Indeed, very satisfactory results have been reported for it when used in conjunction with castor oil, quinine, and pituitrin.^{2, 3, 4} Of all the non-medicinal methods of induction, it is probably the simplest since anesthesia and special apparatus are not required. Its use entails hardly any more danger of introducing infection than does an aseptic vaginal examination, perhaps even less because of the cleansing effect of the escaping fluid. In addition, no foreign body is left in the uterus for twenty-four hours or more as is the case with the bag and the bougie. Moreover, the method in some respects is imitative of nature, resembling those cases in which the onset of labor follows the spontaneous rupture of the membranes. However, the method has certain limitations and contraindications, the extent and nature of which it is the purpose of this report to indicate.

Shortly after the publication of the work of Guttmacher and Douglas,³ it was decided to try their method on a primigravida who was three weeks overdue. She had already had two unsuccessful attempts at induction by means of castor oil, quinine, and pituitrin according to Watson's technic. After a preliminary dose of castor oil and quinine, the membranes were stripped and punctured. Pains commenced in one hour and labor terminated spontaneously twelve and one-half hours later. This excellent result served to encourage further trial of the method. The remaining cases consisted of 25 multiparas at or near

term (thirty-one to forty-one weeks). Of these, 12 had been admitted to the hospital with false pains but were normal in every other respect. The other 13 patients were induced for the following reasons:

Toxemia of pregnancy	6
Organic heart disease	2
Overdue	1
Pyelitis	1
Habitual death of the fetus	1
Thrombosed varicose veins	1
Cardiac neurosis	1

TECHNIC

The following course was carried out preliminary to stripping and rupture of the membranes: 7 A.M. castor oil (2 ounces); 8 A.M. hot soap-sud enema; 9 A.M. quinine (10 grains).

Within two to six hours after the quinine, the patient was placed on the table in the lithotomy position. The thighs and pubic region were shaved and cleansed with green soap and 1 per cent lysol solution. The preparation of the patient was completed with the vaginal instillation of 3 ounces of mercurochrome. In the later cases, green soap was substituted for the mercurochrome and, finally, even the green soap was eliminated. No appreciable difference was noted when mercurochrome, green soap, or nothing was used. In the one case in which there was a mild post-partum infection, mercurochrome had been employed.

Under strict aseptic precautions, one or two fingers were gently passed through the cervical canal and the membranes were stripped off the lower uterine segment as far as the finger could reach. The bag of waters was then perforated with an ordinary sharp-pointed orange stick. As much fluid as could be made to escape without undue effort was slowly released (usually about 250 to 500 c.c.). However, the success of the method apparently did not depend solely upon the quantity of fluid released. In one case in which no fluid escaped although the membranes were perforated (the fetal scalp could be felt distinctly through a definite opening in the membranes), pains began in fifteen minutes and labor terminated spontaneously four hours later. In this case the induction must be attributed to the preliminary medication and the stripping of the membranes.

It was not necessary to employ anesthesia in a single case nor was any appreciable difficulty encountered in perforating the membranes. In several cases, not included in this series, the membranes were stripped but not ruptured because the fetal head was floating, and it was feared that prolapse of the cord might result. With the exception of one breech, all the cases were vertex presentations. No twins were encountered. The method was not used in primiparas, except in the first case of the series, because it was felt that a dry labor would increase the possibility of cerebral birth trauma. Nor was the method employed in multiparas in whom any doubt existed regarding delivery per vaginam. Pituitrin was used in only one case which had a greatly prolonged latent period. It was not used routinely because Gutmacher and Douglas³ showed that it did not appreciably shorten the length of the latent period, the latter being the period of time from rupture of the membranes until the onset of labor pains.

RESULTS

Although labor will always set in after the bag of waters is ruptured, the latent period may be so prolonged that the induction can hardly be considered successful. An efficient method of induction must produce

results within a relatively short period of time. With this in mind, twenty-four hours has been chosen as representing a reasonable maximum latent period.

The *latent period* in this series ranged from ten minutes to fifty-seven hours. Twenty patients went into labor within twenty-four hours, giving an efficiency of 80 per cent for this method. The remaining 5 cases had latent periods of 26, 38¼, 42½, 55¼, and 57 hours respectively. In these cases, the castor oil-enema-quinine sequence was repeated after 24 and 48 hours. In the 57-hour case, two subcutaneous injections of 3 minims of pituitrin half an hour apart were necessary to start labor. No constant relationship could be established between the length of the latent period on the one hand and the duration of pregnancy, age, color, parity, or quantity of fluid released on the other. One patient died fifteen minutes after membrane rupture and was not considered in relation to the duration of the latent period or of labor.

The *duration of labor* was fifteen hours or less in 24 out of 25 cases (96 per cent), which is well within the average range for normal labors. The remaining patient had uterine inertia. Induction was begun two weeks prior to term on the assumption that the case belonged to the group designated as "habitual death of the fetus." This patient had stillbirths in her two previous pregnancies. Labor began after a latent period of one and one-half hours but the pains were weak and occurred at intervals of twenty minutes throughout the labor. After forty-eight hours of this slow-motion labor, it was decided to interfere lest the mother become exhausted. The cervix was now almost fully dilated and labor was easily completed by low midforceps. A living baby was obtained. The placenta was retained for five and one-half hours when it separated spontaneously. This was the only operative delivery in the entire series.

The great majority of the patients had rather short labors. Three delivered in less than one hour after the onset of pains, 7 in less than two hours, 16 in less than five hours, and 21 in less than ten hours. Thus 64 per cent delivered within five hours and 84 per cent within ten hours, which bears out the statement made by Slemmons¹ that the average duration of labor is shortened when this method of induction is used.

Fetal Mortality.—There were 3 fetal deaths or a gross mortality of 12 per cent. The first was a premature infant of thirty-one weeks' gestation. Its mother had essential hypertension with hypertensive encephalopathy. The baby lived only one day. Autopsy revealed no pathology and the death was attributed to prematurity.

The second death was due to prolapse of the cord. This occurred immediately after the membranes were ruptured. Attempts to replace the cord were unsuccessful. Labor was induced in this patient at the thirty-sixth week for essential hypertension with hypertensive retinopathy.

The third fetal death occurred in a patient with rheumatic heart disease, who was induced three weeks prior to term. The duration of labor was seven and one-half hours. The infant died four hours after a spontaneous delivery and autopsy revealed an extensive tentorial hemorrhage without laceration. This was attributed to a rapid dry labor in a premature infant.

Fetal Morbidity.—None.

Maternal Mortality.—There was one maternal death in this series of 26 cases, giving a mortality of 3.9 per cent. The patient was a white woman, forty-two years old, grav. vi, para v, who had essential hypertension and hypertensive heart disease. She was admitted to the hospital three weeks before term with a blood pressure of 180/120. During the two days prior to admission, she had four mild

attacks of dyspnea accompanied by cough and cyanosis. The sputum in the last attack was streaked with blood. These symptoms were promptly relieved by the upright posture. The heart was markedly enlarged to the left, the second aortic sound was accentuated, and there was a systolic blow at the mitral area.

The patient was kept in bed for twenty-four hours and during this period she presented no signs of cardiac decompensation. It was decided to induce labor at this time. With the patient in the lithotomy position, the membranes were ruptured. Immediately following the escape of about 500 c.c. of amniotic fluid, she suddenly became markedly cyanotic, dyspneic, and pulseless. This was accompanied by a violent cough productive of large quantities of blood-tinged frothy fluid. Loud moist râles indicative of pulmonary edema were very evident. Despite all therapeutic efforts, including venesection and atropine, the patient died fifteen minutes after the onset of the pulmonary edema. Consent for autopsy was refused.

Maternal Morbidity.—There was only one postpartum infection and this in a colored patient who ran a febrile course for four days following delivery. The maximum temperature was 103.2° and the lochia was very foul. The patient made an uneventful recovery. In this case, mercurochrome had been used as a vaginal antiseptic. The latent period was forty-two and one-half hours and the total duration of labor was two hours.

The remaining complication occurred in a white patient, twenty-eight years old, grav. ii, para i. She gave a history of "growing pains" at the age of thirteen but there were no cardiac symptoms until her first pregnancy thirteen years later (1930). She had mitral stenosis and insufficiency with auricular fibrillation, Class III. Although she was in marked cardiac failure during this pregnancy, she made a good recovery following delivery.

The patient returned to us two years later (1932) in her second pregnancy and was admitted to the hospital about two months before term. She was kept in bed and fully digitalized. During this period of observation she presented no signs of decompensation or of an active rheumatic infection. It was decided to induce labor three weeks before term. With the patient in the sitting position, the membranes were ruptured and a rather large quantity of fluid escaped (about 750 c.c.). Almost instantaneously, the patient became very cyanotic and dyspneic. Numerous loud bubbling râles were audible throughout the chest and the frothy sputum that streamed from her mouth was streaked with blood. One hour later, she was comfortable again, having derived considerable relief from oxygen inhalations, morphine, and the upright sitting position. Venesection was not performed. No râles could be heard the following day. Labor began after a latent period of thirty-eight and one-fourth hours and terminated spontaneously seven and one-half hours later. There was no recurrence of the pulmonary edema or of any other signs of cardiac insufficiency during labor or the puerperium.

DISCUSSION

The main objections that have been made to membrane rupture as a means of inducing premature labor are that it is uncertain and slow, that it carries a greater likelihood of fetal trauma, and that there is increased danger of sepsis. In the first place, none of the present non-medicinal methods is free of any of these disadvantages. In regard to efficiency of induction and incidence of infection, membrane rupture compares very favorably to the bag and the bougie.³ The question of fetal injury in a dry labor is very interesting but rather difficult to settle. The large number of cases already reported of artificial rupture

of the membranes for induction of labor shows that in uncomplicated cases the hydrostatic dilating wedge is not as important as previously regarded.^{5, 6} Of course, the fetal injuries observed in dry labors associated with a contracted pelvis, large baby, or abnormal position should not be entirely attributed to the absence of the bag of waters. Preservation of the bag of waters is certainly desirable in these pathologic labors but its presence is of secondary importance. Usually, the membranes rupture spontaneously early in this type of labor so that the question is more often of academic than practical significance.

The unusual experience encountered in the two cardiac patients of this series would seem to indicate that membrane rupture is too dangerous a method for the induction of labor in patients with heart disease. Although one hesitates to draw sweeping conclusions from so limited an experience, the dramatic suddenness of the appearance of pulmonary edema following rupture of the membranes was, perhaps, too impressive to be considered only a coincidence. The acute cardiac collapse is probably related to the sudden and marked reduction of intra-abdominal pressure, a change that is more profound in cardiac patients than in normal pregnant women because of the relative hydramnios often associated with heart disease. Reports of others who have had experience with this method in cardiac patients should be very valuable.

SUMMARY

1. A series of 26 cases of induction of labor at or near term by stripping and rupture of the membranes is reported. The technic of induction included a preliminary course of castor oil, enema, and quinine.

2. The results of this study show an efficiency of 80 per cent, maternal morbidity of 7.6 per cent, maternal mortality of 3.9 per cent, and a fetal mortality of 12 per cent. There was no fetal morbidity.

3. The high maternal morbidity and mortality were chiefly due to the development of acute pulmonary edema in the two cardiac patients of the series.

4. Although this method of induction of premature labor has certain advantages not possessed by other methods, its use in patients with organic heart disease appears to be rather dangerous.

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THE INADEQUACY OF EXTERNAL PELVIMETRY*

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IN THE present paper I wish to confine my remarks to external pelvimetry and to consider especially the four maneuvers that are employed as a routine procedure by most obstetricians. I refer to the determination of the length of the interspinous diameter, the intercrystal diameter, the intertrochanteric diameter and the external conjugate or Baudeloque's diameter. That these procedures are wholly inadequate for determining the true diameters of the pelvic inlet becomes increasingly evident to me as our work in roentgen pelvimetry progresses. Furthermore the measurements obtained by external pelvimetry may be misleading. This is no new conception. Ever since the time of Baudeloque various observers have questioned the value of these procedures. Criticism has been directed especially toward the method of determining the length of the true conjugate by the subtraction of certain figures from the length of the external conjugate.

Dohrn¹ in 1867 in discussing the relation between the length of the diameters of the external and true conjugate stated that his results confirmed the conclusions of Michaelis, Crede and Schröder. He was of the opinion that in the flattened pelvis the figure to be subtracted from the external conjugate in order to obtain the length of the true conjugate varied greatly and that in general the length of the external conjugate diameter could not be regarded as an index of the length of the true conjugate. In the same year Schröder² stated that the method of Baudeloque is of no particular value in diagnosing narrow pelvis and that the deduction to be made from the external conjugate varies extremely. In his series of 68 pelvises, 28 normal and 40 abnormal, the figure to be deducted from the length of the external conjugate diameter ranged from a minimum of 6.4 cm. to a maximum of 10.0 cm. The number of centimeters to be subtracted depended upon the type of pelvis, thus; the flat pelvis necessitated the greatest deduction and the generally contracted type the least. Skutsch³ has shown in reviewing 100 pelvises that the difference between the lengths of the external and true conjugate varied from 5.5 cm. to 10.0 cm. and Baisset⁴ in a study of 120 dried pelvises arrived at the same conclusions. Goenner⁵ in 1901 stated that measurements obtained from dried pelvises apparently are too large for statistical purposes. He reached this conclusion from the fact that the pelvises of 100 cadavers when classified according to the usual standards of measurement fell generally into the contracted group. It was quite obvious to him that external pelvimetry alone yielded little or no information re-

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garding the true length of the transverse diameter of the superior strait. Finally Sheffer⁶ showed that the transverse diameter of the inlet may be equal in two pelves while the lengths of the intereristal diameters vary by 3.3 cm. In our clinic where particular attention has been given to the variations present in the transverse diameter of the superior strait and their influence upon the course of labor, we have never been able to determine any uniform relationship between the lengths of the transverse diameter and the intereristal diameter.

At this point I wish to direct attention to the accuracy of the roentgen method which we employ in measuring the superior strait. This procedure has been considered again in detail in a recent publication to which those who are interested are referred.^{7, 8} We are satisfied that the method is accurate to within 2 mm. which from a clinical point of view is all that necessity demands. The method has been repeatedly checked on dried pelves and in patients at laparotomy in this clinic and by other observers. Line projections and shadowgraphs have been used to determine how much individual variation is possible on the part of the observer before errors become significant. With respect to this point we are convinced that the method in average hands (i.e. a technician in roentgenology) is accurate to within 2 mm. Furthermore the great simplicity of procedure and the rapidity with which results may be obtained has made the method of almost daily usefulness in our hands.

In this communication a review is presented of the external measurements in 75 pelves which have also been measured by roentgen pelvimetry. A study of the series discloses the following information:

The maximum anteroposterior diameter of the superior strait was 14 cm.
 The minimum anteroposterior diameter of the superior strait was 7.75 cm.
 The maximum external conjugate diameter was 22.5 cm.
 The minimum external conjugate diameter was 16.0 cm.
 The maximum difference between the external and true conjugate was 10.0 cm.
 The minimum difference between the external and true conjugate was 5.5 cm.

We observe from the foregoing figures a difference of 4.5 cm. in the subtraction necessary to determine the length of the true conjugate from the length of the external conjugate diameter. A few examples from the series show how wide the variation may be.

	SPINES	CRESTS	TROCH.	EXT. CONJ.	TRUE A.P.	TRUE TRANS.
Case 49	24.0	27.0	30.0	20.0	10.0	12.75
Case 52	20.0	24.0	28.0	16.0	10.0	10.75

In the two foregoing cases the lengths of the two external conjugate diameters differ by 4 cm. yet the true anteroposterior diameters are identical.

	SPINES	CRESTS	TROCH.	EXT. CONJ.	TRUE A.P.	TRUE TRANS.
Case 54	23.0	25.0	---	17.0	7.75	13.0
Case 53	24.0	28.0	29.0	17.0	11.0	10.75

These two cases present abnormal pelves with identical external conjugate diameters; that of Case 54 is definitely a simple flat pelvis probably rachitic. The patient was delivered by cesarean section. Case 53 is a true dolichopellic pelvis. The fetus presented with the occiput posterior, a presentation which we have learned to foresee in this type of pelvic inlet.

	SPINES	CRESTS	TROCH.	EXT. CONJ.	TRUE A.P.	TRUE TRANS.
Case 37	22.0	24.75	29.0	16.75	11.0	12.5
Case 41	21.0	24.0	28.0	18.0	11.5	11.5

The pelves of Cases 37 and 41 according to the grouping presently employed would be classed on the basis of external measurements as generally contracted pelves yet the internal measurements show adequate pelves with no general contraction. The former was delivered by low forceps of a fetus weighing 3256 gm. and the latter spontaneously of a fetus weighing 3340 gm.

Any discussion of pelvimetry should include a consideration of the most important manual maneuver we possess, namely, the determination of the diagonal conjugate diameter. It is surprising as I survey our series how many times the letters N. R. (not reached) appear under this caption. I think most men of experience will agree that when this measurement is attempted in certain primiparas without the use of anesthesia difficulties may arise. The shortness of the examiner's fingers, the difficulty of introducing both fingers into the vagina and the resistance of the perineum are all factors which may prevent the success of the maneuver. Furthermore the same difficulty arises here as with that of evaluating the external conjugate diameter, namely, the determination of the figure to be deducted in order to obtain the true conjugate. The thickness, height, and inclination of the symphysis are all factors which add to the difficulty of obtaining accurate results. Even when the procedure is apparently useful we still lack information as to the character of the transverse diameter of the pelvis, in my mind a diameter which is assuming more and more importance as we study its variations.

One hesitates to express an adverse opinion concerning the time-honored custom of taking external pelvic measurements, yet the facts revealed by roentgenographic studies are impressive and significant. Certainly *to classify pelves by means of the four external measurements usually taken is erroneous and illogical*. Furthermore the question may well be raised whether in the absence of roentgenometric methods external measurements are at all valuable. I must confess that they mean very little to me. It is true that when I find an external conjugate diameter of 18 cm. or less I entertain the possibility of pelvic contrac-

tion but beyond this point I am unwilling to go. In conclusion I must again state my firm belief that scientific obstetrics demands an accurate survey of the pelvis of every primiparous woman, and this ideal may be obtained by only roentgenometric methods.

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A SIMPLE DEVICE FOR RUPTURING MEMBRANES

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IF THE end of an ordinary thimble, preferably of silver, be cut with a file through the center in two places and the sector raised to form a claw, it will be found useful as an instrument for rupturing the membranes either to initiate labor or during its progress. The device may be worn upon the first or second finger of

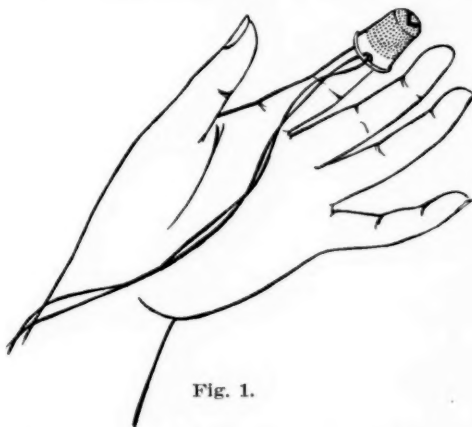


Fig. 1.

the examining hand with the claw pointing forward. As a precaution against slipping off and also to indicate the point of direction of the claw, a small hole is bored at the base for the attachment of a stout silk thread. This instrument may be used by touch and there is much less likelihood of unintentionally injuring mother or infant than with scissors or other sharp pointed instruments which in the past have been recommended.

A NEW METHOD OF READING THE FRIEDMAN MODIFICATION OF THE ASCHHEIM-ZONDEK TEST

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THE Aschheim-Zondek test has come to be generally recognized as a very reliable reaction for the early diagnosis of pregnancy. Friedman's modification, the use of rabbits instead of mice as the test animals, has retained the accuracy of the original test, and has greatly simplified the technic of the test. It has also reduced the time necessary for determining the result of from twenty-four to thirty-six hours. A further reduction of time would be very valuable in certain cases, particularly where a question of ectopic pregnancy arises. We believe that such a method is now available. This new method also greatly simplifies the technic of the test by obviating the necessity for operating upon the animals.

In 1930, Bereovitz reported certain studies on the pupillary reactions of pregnant and nonpregnant women when a few drops of their own serum was instilled into the conjunctival sac of one eye, under proper lighting conditions, the other eye being used as a control. In the nonpregnant women there was no change in the tested pupil.

In performing the Friedman modification of the Aschheim-Zondek test by the routine technic, one of us (Konikov) suggested that we record the pupillary reaction of the rabbit immediately after injecting the urine into the marginal ear vein, and then check the result by the accustomed operation upon the animal. Our results on 250 cases are given in Table I.

TABLE I. TABLE INDICATING THE PUPILLARY REACTIONS OF THE RABBIT IN PREGNANT AND NONPREGNANT PATIENTS

	TOTAL	POSITIVE	PER CENT	NEGATIVE	PER CENT	DOUBTFUL	PER CENT
Pregnant	154	134	87.0	17	11.0	3	2.0
Nonpregnant	96	14	14.6	77	80.2	5	5.2

If Table I is regarded from a different point of view, it is seen that a positive report is correct in 134 of 148 reports (90.6 per cent), and a negative report in 77 of 94 reports (81.8 per cent).

The pupil of the rabbit reacts in a variety of ways. It will frequently contract to a size of about 2 mm. while the urine is still being injected. In most cases, however, the pupils in the positive cases will

react in from one to five minutes, the contraction lasting from one to ten minutes. The dilatation of the pupil occurs in the same manner.

In reading the test, certain errors have undoubtedly crept into the work which have been recorded as such, but which have contributed somewhat to the lowering of the accuracy of the readings. In the first place, we read as positives only those cases which had a decided contraction of the pupil, paying no attention to dilatation of the pupil until one of us (Davis) suggested that this also be recorded as positive. Among the last 125 cases, there have been 15 in which a dilatation of the pupil occurred, and the test was positive on operation on the animal. This error undoubtedly accounts for a few of the false negative reports. With reference to the false positive reports, we have no explanation at the present time, except that eight of them occurred at about the same time on one group of eight rabbits which came into the laboratory together.

We have also injected known negative urines into rabbits which were found positive at operation, and have secured negative results by the pupillary test. These injections were immediately followed by injections of known positive urines, and positive pupillary reactions followed. After the pupils of the rabbits in the latter cases had returned to normal, they were reinjected with known negative urines, and negative results were secured by the eye reaction.

It is thus seen that this method, while not yet as accurate as the original technic, will still be of value in cases where an immediate report would be of great clinical importance. We ourselves still continue to operate upon our animals before giving out reports on the test, because of the greater accuracy of the latter method. In three cases, however, where ectopic pregnancy was suspected clinically, the pupillary reaction test was confirmed in all three cases when it gave two positive and one negative reports. It is hoped that the technic will be improved by ourselves or others so as to give an accuracy more nearly approximating that of the operative method, thus greatly simplifying the test, reducing the time required for rendering a report, and also lowering the expense of the test.

CHORIONEPITHELIOMA OF THE FALLOPIAN TUBE

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NÜRNBERGER'S comprehensive and critical review (1932) of the literature on tubal chorionepithelioma, differing slightly in the recognition accorded certain case reports included in the earlier reviews of Robert Meyer (1930), Dietrich (1926), and others, cites 33 bona fide descriptions of this tumor to 1932. Since the publication of Nürnbergger a further case has been reported by Stein. The following case, observed in Siam, appears to belong to the foregoing group of chorionepitheliomas. If it be acceptable as a valid example of this type of growth, it possesses an added interest in being, along with the cases of Albert and de Senarclens, among the largest tubal chorionepitheliomas thus far described.

CASE.—Nang R., Siamese, aged thirty, had twice previously been pregnant. Normal labors had ensued, the last occurring two years ago. Previous medical and menstrual history irrelevant.

The patient was admitted in April, 1932, complaining that the menses had been irregular for thirteen months. These irregularities had been as shown in Fig. 1,

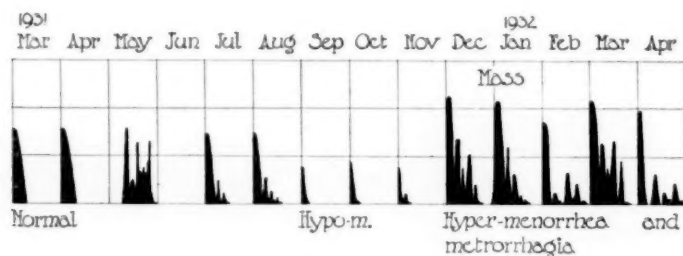


Fig. 1.—Menstrual record.

and had not been accompanied by symptoms of pregnancy nor indeed by symptoms of any kind whatsoever until four months before admission. At that time a painful swelling had appeared in the left lower abdomen. The swelling had meanwhile grown rapidly, and the patient had lost much weight and strength. No tissue had been passed per vaginam at any time during the irregular bleedings.

On examination, the patient was found cachectic and the pulse was 130. The general physical examination and routine laboratory findings were otherwise not pertinent. Abdominal examination showed a tender, movable cystic tumor the size of a six months' pregnancy having a basal attachment in the left lower quadrant. There was evidence of a small amount of free fluid in the abdomen. The vaginal examination showed a small amount of dark, unclotted blood issuing from the os uteri. The vaginal and cervical appearances, however, were not suggestive of pregnancy. The cervix was small and firm, and the external os practically closed. The corpus uteri was also small and firm, and was displaced slightly to the right by the large left adnexal cystic mass. The right ovary was indefinitely palpable.

The provisional diagnosis was "malignant ovarian cyst." After preliminary supportive therapy the patient was submitted to exploratory laparotomy.

Operation.—The peritoneum contained a moderate amount of serosanguineous fluid. The tumor consisted of a dark, very irregularly surfaced and friable cyst, the walls of which were about 2 cm. in thickness. Aspiration for the purpose of reducing its bulk yielded over two liters of dark and blood-stained serous fluid. It was then found to be attached by a narrow pedicle to the outer end of the left tube, with light adhesions to the adjacent parametrial and pelvic peritoneum above and below the brim of the true pelvis on this side. The omentum was broadly adherent to the upper pole of the tumor. Except in the latter features the peritoneum was not otherwise involved, nor was any gross "seeding" apparent; the peritoneal adhesions in the pelvic area separated readily without unusual oozing. The left ovary, moderately enlarged and cystic, hung freely beneath the lower pole

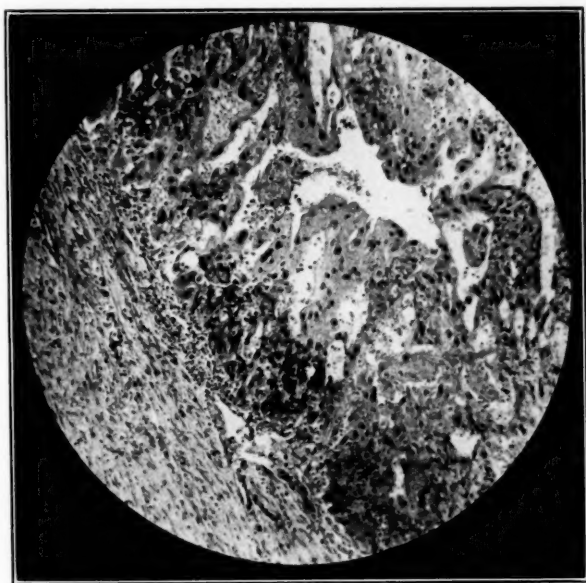


Fig. 2.—Section of tumor showing both the Langhans and syncytial type of cell. (Zeiss obj. 8; ocular 10.)

of the tumor. The right ovary was also, but less distinctly enlarged and cystic. The uterus was small, firm and apparently normal.

In the belief that a malignant fimbrial cyst was the explanation of the findings, operation was confined, in the patient's weakened condition, to simple supracervical hysteroadnexectomy.

Gross Pathologic Specimen.—The specimen removed at operation consisted of a degenerate and friable shell of tissue, resembling in color and texture the features of the maternal surface of a full-term placenta. Here and there on the surface of cyst wall, however, remnants of a serous capsule were recognizable. The outer end of the left tube was fused in the cyst wall, a patulous abdominal ostium was not located. The opposite tube was normal. The uterus was small and firm, its walls slightly thickened. The endometrium was velvety in appearance, clean except for a few punctate hemorrhagic spots, and was approximately 4 to 5 mm. in thickness. The left ovary was enlarged to about three times normal size by the presence of

multiple cysts containing straw-colored serous fluid and lined by yellow lutein tissue in certain instances, indeterminate opalescent grayish tissue in others. The right ovary was similarly affected but was approximately only double its normal size.

Histologic Examination.—Sections of the tumor showed, for the most part, a thick matrix of poorly staining degenerate tissue of unknown type. Here and there throughout this framework, however, were irregular masses and cords of viable neoplastic tissue taking the stains well, and indisputably chorionepitheliomatous in character. The syncytial type of chorion predominated but peripheral masses of smaller, well circumscribed and actively proliferating cells were also seen. The latter had well outlined cell membranes, a less acidophilic cytoplasm than the syncytial masses, and small, pale but sharply bound nuclei with large nucleoli and occasional mitotic figures. Inflammatory cells were numerous (Fig. 2).

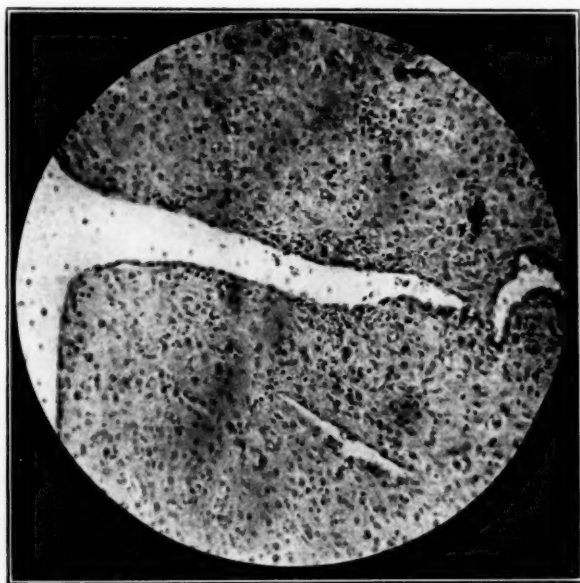


Fig. 3.—Endometrium in tubal chorionepithelioma. The deciduous character of the functional stroma and the scarcity of glandular figures are notable. Zeiss obj. 8; ocular 10.

The endometrium was 4 to 5 mm. in thickness. Its surface was covered by a low cuboidal type of epithelium. The stroma of the functional two-thirds was loose and deciduous in character, though not unusually congested. With the exception of certain large sinuses opening upon the uterine cavity, this portion was almost entirely lacking in characteristic glandular figures. The latter were mainly confined to the still compact basal layer of the endometrium, where a few tortuous stumps resembling in shape the pregravid type of gland were visible (Fig. 3).

The ovaries showed several large, cystic persistent follicles, but for the most part were occupied by cysts exhibiting an irregular type of luteinized cell lining. Such lutein layers as were observed were disposed in patchy areas, the cells rather degenerate in appearance. Fibrous thecal "organization" was limited here and there to attenuated strands of tissue overlying the inner surface of the lutein layers (Figs. 4 and 5).

Further Observations.—While the immediate postoperative course was uneventful, and no metastases were discoverable at the time these notes are recorded, the case has been too recently treated to report a final result.

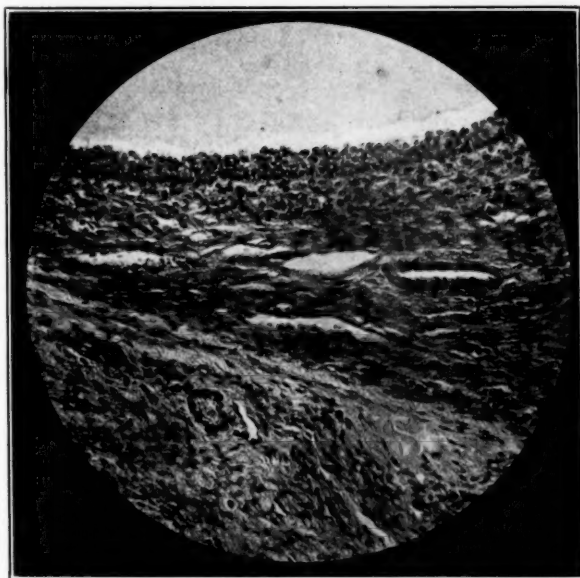


Fig. 4.—Ovary in tubal chorionepithelioma. Over-ripe and cystic follicle, with beginning hyperplasia of theca interna layer. Zeiss obj. 8; ocular 10.

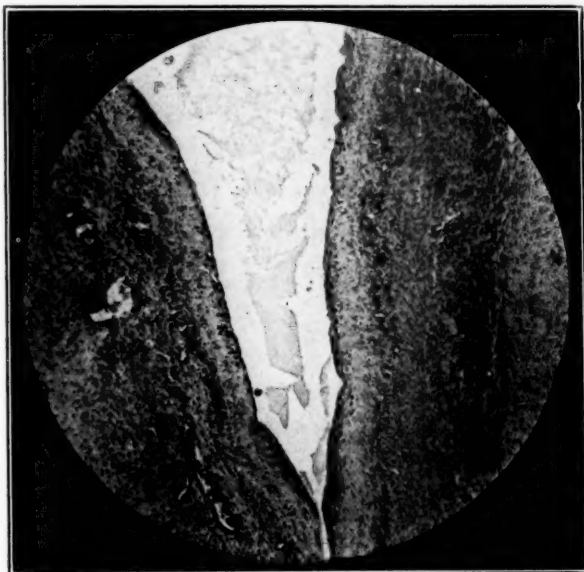


Fig. 5.—Ovary in tubal chorionepithelioma. Atretic lutein cystoma; early hyalinization of the thin lutein cell layer and hyperplasia of the theca interna. Zeiss obj. 8; ocular 10.

A specimen of *urine*, collected postoperatively and preserved with a glycerin-phenol mixture, was brought to Europe and there tested* by the Aschheim-Zondek

*We are indebted to Prof. Hugo Sellheim of Leipzig for courtesies extended in this and in the study of case specimens.

method in June, 1932, or about five weeks after being voided. Quantitative examination showed it still contained at that time a concentration of anterior pituitary hormone in excess of 250,000 mouse-units per liter.

Comment.—From the theoretical standpoint *primary* tubal chorionepithelioma may be possible of origin according to one of three methods: (1) It may arise at the implantation site of a tubal pregnancy in a manner analogous to its origin at intrauterine sites. Many of the tubal chorionepitheliomas thus far described appear to have had this so-called "orthotopic" type of pathogenesis. (2) As an "ectopic" growth the tumor may arise by the malignant transformation of benign or molar chorionic emboli, lodged in the tubal vessels after deportation from an intrauterine, or other site of primary nidation. The theoretical grounds for this type of pathogenesis are still a subject of discussion; the actual demonstration is beset with many obvious difficulties. (3) The third possibility is a teratomatous or teratogenous origin.

Metastatic tubal chorionepithelioma may present the appearance of an isolated and primary tubal neoplasm if the true primary tumor, for example in the uterus, has been expelled, resorbed, or overlooked. Reports of the disappearance of such primary intrauterine tumors are not only numerous, but appear now to be well authenticated.

The theoretical and practical difficulties underlying the demonstration of an indisputably primary tubal chorionepithelioma are thus readily appreciated.

In the present instance certain evidence needed for offering the case as an example of such a primary growth is unfortunately lacking. The inconclusive history and the prolonged delay prior to hospitalization are both unavoidable handicaps attending work among Oriental patients. The atypical menstrual protocol by no means excludes, however, the possibility of an original ectopic pregnancy. It is moreover possible that the long neglect of the process was responsible for failure to identify beyond question the basic relationship between tumor and tubal ostium, as attempted through serial sections. In spite of these deficiencies it is believed that the remaining evidence is sufficient to suggest that the growth is a primary tubal chorionepithelioma, apparently arising as an "orthotopic" tumor on the site of a previous tubal pregnancy.

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221 NORTH SIXTH STREET

VESICAL SYMPTOMS IN THE FEMALE

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VESICAL symptoms of varying grades of severity, frequently encountered in adult women, arise from causes so varied and occasionally so serious as to warrant our sharpest attention.

In a recent review of 500 of my female patients, vesical symptoms were complained of in 143, or 28.6 per cent. This impressed me as something worthy of investigation and, if possible, prevention.

In 96 of my patients, or 67.1 per cent of those with vesical symptoms, bladder disturbances existed for three months or more before relief was sought. The delay in most cases was due either to modesty or to first employing various panaceas, the patient presenting herself only when the discomfort had become intolerable.

The most common symptom in the group, irrespective of pathology or cause, was *frequency*, which was present in over 90 per cent of the patients. It varied in degree up to complete incontinence, and was usually associated with one or more other symptoms.

Dysuria or painful urination was a common finding, occurring in 78 or 55.2 per cent of the cases. It occurred at any period in the act of micturition, although it was most severe after the beginning and at the end. The type of pain varied from a mild burning sensation to the terrific pain of vesical spasm, when the mere thought of voiding became a mental torture. In the severer local inflammations, the tenesmus was followed by a perineal aching pain which persisted until the next voiding.

Retention occurred in 12 or 8.4 per cent of the group. This does not begin to represent its frequency, for the nervous or psychogenic retention after abdominal or perineal operations, or even normal delivery, is a common observation. Those observed in this group were mostly due to impaction of pelvic tumors, and incarcerated retroverted pregnant uteri, although one was due to papilloma of the bladder, and one to malposition of a Gehrung pessary.

Incontinence completes the tetrad of the most common vesical symptoms, and this was noted in 42 or 29.4 per cent of the affected group. It was partial and manifest only on coughing, passing flatus, sneezing, and laughing, in all but 7 or 4 per cent, and in these it was complete, with constant dribbling.

Hematuria and pain over the bladder were complained of by only 3 and 5 patients, or 2.1 per cent and 3.5 per cent, respectively.

In seeking the pathologic source of the symptoms, careful history-taking and physical examination rank first in importance. The tendency to seek the most probable source of symptoms should not totally obscure the possibility of diabetes, tabes, nephritis with hypertension, or a normal pregnancy. Infections elsewhere in the genitourinary tract, such as pyogenic and tuberculous renal infection, renal and ureteral calculi, and strictures, are prolific causes of vesical symptoms. In conducting an examination, the first local sign to search for is purulent vaginal, urethral, or adjacent duct discharges. The presence or absence of pus and its exact locations are noted and the patient is instructed to "bear down." If present, a cystocele, urethrocele, or patulous urethra with paralyzed or injured sphincter will then be evident. A urethral caruncle is a common offender, as well as a *Trichomonas vaginalis* discharge. Gross lesions, such as submeatal fissures, urethral malignancy, and vaginal fistulas, are readily detected.

The existence of urethritis, diverticula, and foreign bodies of the bladder naturally give rise to marked vesical symptoms as does also a trigonitis of gonococcal or colon bacillus origin. The latter is often overlooked in doing pelvic operations. A Hunner ulcer which had long escaped detection, was the cause of one most intractable case. Another was due to multiple minute ulcers on and near the trigone, directly traceable to teeth infection. A patient operated upon for cystocele failed of cure because of a relaxed sphincter vesicae. When the latter was repaired, the patient again had normal bladder control. This defect in the primary operation is a too common cause of subsequent bladder "weakness."

Bimanual examination permits palpation of the urethra and base of the bladder, and other pelvic sources of the pathologic condition. Two types of pelvic offenders are of concern: First, tumors or pelvic organ displacements causing external vesical pressure, and second, pelvic inflammatory disease extending through contact to the bladder and ureters. The pregnant and anteverted uterus not only impinges upon the bladder but also causes a passive congestion which predisposes to infection. If retroverted, acute retention occasionally results.

Benign tumors of the uterus, such as fibromyomas, ovarian tumors, and inflammatory masses, likewise lessen bladder capacity and cause stasis in the enlarged vessels accompanying the lesion. But since pelvic tumors, when present, do not necessarily give rise to vesical symptoms, the interior of the bladder should always be inspected in such cases before operation. One such embarrassing oversight in this series has thoroughly impressed this upon me. The coincidence of bladder symptoms with acute or abscessed appendicitis is too well known to require comment.

Recognition of overflow incontinence after parturition or operation is often delayed until the patient is greatly distressed and the bladder completely paralyzed. Vesical irritability and frequency are common sequelae to rupture of the urogenital diaphragm, with relaxation and descent of the urethra and trigone.

Cystocele, one of the commonest causes of vesical incontinence, is largely preventable by proper care during and after parturition. A filled or partly filled bladder during parturition is responsible for a majority of cystoceles, through damage to the urogenital diaphragm and pubovesical fascia. Frequent catheterization when distention is visible or suspected is the only prophylactic, and always to be employed before operative termination of the second stage of labor. An episiotomy or perineotomy is the greatest savior of pelvic structures during parturition. It relieves pressure on the urogenital diaphragm and prevents the small numerous tears in the levator ani, pubovesical, and rectovesical fascia, which are often present without visible vaginal or perineal lacerations. It is especially indicated in primiparas with long perineal body, narrow pubic arch, or oversized fetus. In the thirteen patients in this series having cystocele with vesical symptoms, only one has had a perineotomy performed. Eight followed "instrumental delivery" and 5 patients said their parturition had been normal.

COMMENT

1. Bladder symptoms were present in 143 or 28.6 per cent of 500 female patients seeking consultation.

2. Of these patients 115 or 23 per cent had definite pathologic lesions responsible for their symptoms.

3. In a few cases, the most obvious pathologic lesion was not the symptom-producing one.

4. An understanding of the physiologic and anatomic data concerning the female bladder instills appreciation of proper prophylaxis during parturition and after operation.

5. The incidence and findings in these patients indicate the need for serious consideration of vesical symptoms in the female.

39 GIFFORD AVE.

GLYCOGEN PRODUCTION IN THE ISTHMUS UTERI

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THE purpose of this paper is to prove an essential difference between the physiology of the isthmus of the uterus and that of the corpus. Oscar Frankl, in his recent work on the isthmus,¹ says: "The mucous membrane of the isthmus is always thinner and contains less glands than the corpus, but may simulate thickening by cystic dilatation of the glands. The mucosa of the isthmus is much less able to respond to hormonal stimuli than that of the body. The premenstrual change may be shown in part in the glands, but very frequently the mucous membrane of the isthmus remains in a state of complete rest." Frankl further states: "The differentiation of the isthmus mucosa is missed already in the beginning, and even more in the advancing interval, while the corpus mucosa shows differentiation into two layers, and at the premenstrual stage into three layers. The isthmus is also less able to respond to pathological hormonal influences than the body."

I have studied the uterine mucous membrane, both corpus and isthmus, from the standpoint of the glycogen content of the epithelium. I have assumed that, if a difference can be shown in this most significant biochemical function (glycogen production and storage), a true physiologic difference exists between the isthmus and the corpus.

Binder and Neurath have made a careful study of the glycogen content of the uterine mucous membrane. In their series of cases they were able to demonstrate finest particles of glycogen in postmenstrual mucous membrane. No case showed glycogen in the first half of the interval. Two specimens from the middle of the interval showed traces in the glands. In 13 sections from the second half of the interval, glycogen was found in all, and in 12 specimens of premenstrual mucous membrane glycogen was found in 11, one being negative. Binder and Neurath refer to the work of Driessen, who found no glycogen in postmenstrual glands, in the interval glycogen as fine droplets in the epithelium, and at the premenstrual stage relatively large amounts of glycogen in the epithelium and the lumina of the glands. Binder and Neurath also refer to Aschheim's work on the subject. This author reports the presence of glycogen in postmenstrual epithelium, but only in those glands which have retained their premenstrual character. He notes that the glycogen content reaches its high point in the premenstrual stage, and at this time, the glandular epithelium seems to overfill, and glycogen is thus found, in the lumina of the glands, and in the musculature and the stroma. Aschheim calls attention to the fact that the superficial glands are glycogen-rich, the deeper ones glycogen-poor or glycogen-free.

Glycogen is present in premenstrual mucous membrane, and it acts as a fertilizer for the ground which is to receive the impregnated ovum. In fact, it would be better perhaps to use the term "pregravid" instead of "premenstrual" mucous membrane, as all histologic and biochemical changes which occur at this stage take place with one end in view: to facilitate the development of the young ovum in the mucous membrane. Until the beginning of nourishment by maternal blood, the ovum is nourished by embryotrophic material. This means by the chemical substances which the ovum finds in the uterine mucosa itself. Glycogen is one of the most important of all these chemical substances.

To determine the presence or absence of glycogen, Best's carmine stain was used. Thirty-one uteri were examined, both corpus and isthmus. The presence of glycogen was noted only in the epithelium and lumina of the glands, the musculature and the stroma being disregarded as unimportant in the solution of the immediate problem. In common

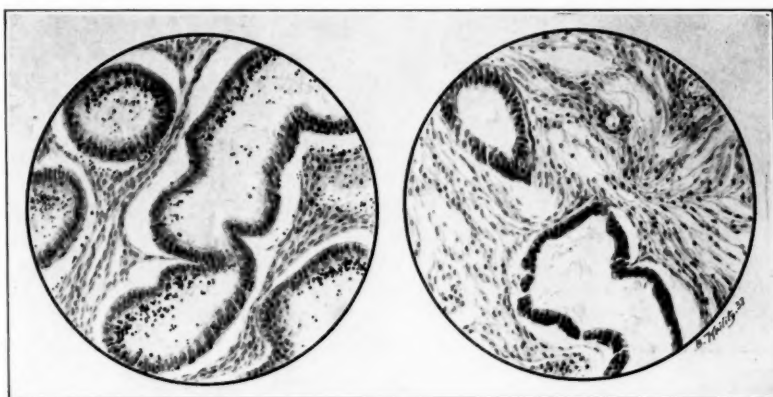


Fig. 1.

Fig. 2.

Fig. 1.—Corpus. Large amounts of glycogen in the epithelium and lumina of glands.
Fig. 2.—Isthmus. Same specimen as Fig. 1. No glycogen present.

with the authors above mentioned, I found, in general, increasing amounts of glycogen as the interval advanced, glycogen being most abundant at the premenstruum.

In seven specimens the mucous membrane was in the beginning or the first half of the interval. No glycogen was found in the corpus or in the isthmus glands. Two cases at the middle of the interval were examined. In one glycogen was found in the corpus glands but not in the isthmus; in the other no glycogen was found. Five cases in the second half or from the end of the interval were examined. Of these glycogen was found in the corpus glands in large amounts in three cases, and in the fourth case scattered through some of the glands, none being found in the fifth. In three of the five cases traces of glycogen were found in the isthmus, in each case, however, the amount was much less than that found in the corresponding body. Seven uteri were

secured with premenstrual mucosa. Of these six showed glycogen in the corpus glands to a degree varying from moderate to superabundant. However, only two of the seven cases showed glycogen in the isthmus, and then the quantities were markedly less than that found in the corresponding bodies (see Figs. 1 to 4). In one section, although the mucous membrane was typically premenstrual, no traces of glycogen could be found. Five cases in the postmenstrual stage showed absence of glycogen in the corpus and in the isthmus. Also three uteri with cystic hyperplasia of the endometrium showed no glycogen. Besides these, ten cases with premenstrual mucous membrane were stained, and all showed glycogen in the epithelium and in the glandular lumina. In these no isthmus was available since the sections were cut from old blocks. Interesting is the fact that throughout my investigations I

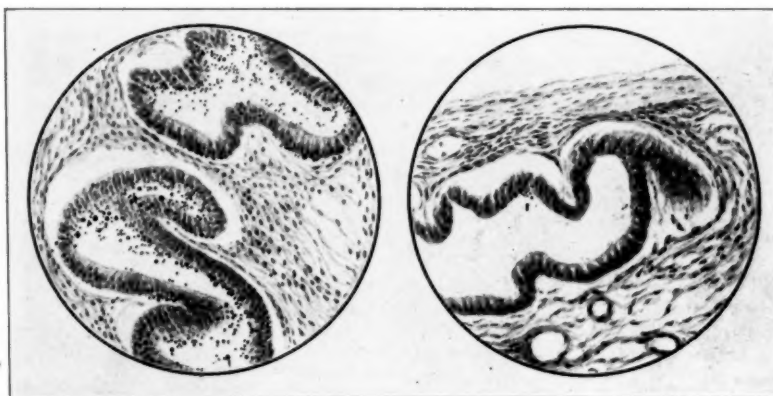


Fig. 3.

Fig. 4.

Fig. 3.—Corpus. Another specimen. Note large amount of glycogen.

Fig. 4.—Isthmus. Same specimen as Fig. 3. Glycogen content small in contrast to corpus.

often found glands loaded with glycogen adjacent to glands which were glycogen-free.

From the above it is apparent that the glands of the isthmus contain at the premenstruum, and the period immediately preceding it, much less glycogen than those of the corpus. We may therefore conclude not only as Frankl has said, that the isthmus at this time often fails to differentiate and hypertrophy, but also that the isthmus does not respond to hormonal stimuli as does the corpus, as shown by the virtual absence of glycogen production and storage. An important clinical fact which may be explained by these findings is the rare occurrence of a real isthmie implantation of the ovum. Above it has been pointed out that in its initial stages of development, glycogen is necessary for oval nourishment. Thus in view of the absence or low glycogen content of the isthmus, we may imagine that the ovum avoids

this area as a result of chemicobiologic forces, or, should it come to rest in the isthmus, its chances of survival are greatly diminished.

The author acknowledges courtesies shown by Prof. O. Frankl, of Vienna, in giving advice and supplying necessary material.

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THYMUS EXTRACT IN LABOR

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IN UNDERTAKING the study of thymus extract in labor, it was originally intended as a comparison with a similar study of a combination of thymus and pituitary extracts, commonly known as thymophysin.¹ It soon became apparent that:

First, thymus extract could stimulate contractions in the human uterus.

Second, these contractions simulated the normal, spontaneously originated, uterine contractions.

These hypotheses immediately gave rise to the questions: Does the thymus gland play any rôle in labor? If so, to what extent and in what manner? In the present paper we shall endeavor to evaluate the use of thymus extract in labor.

For this purpose 50 patients were selected at random. Of these 16 were primiparas; 11 para ii; 4 para iii; 2 para v; and one each para iv, vi and vii. The extent in labor as shown by the amount of cervical dilatation ranged from no dilatation in 4 patients to 3 fingers' dilatation in one. There were 39 occipitoanterior, 9 occipitoposteriors, 1 mentum anterior, and 1 set of twins.

The question of dosage had to be arbitrary. Having at an earlier time employed thymophysin, a combination of thymus and posterior pituitary lobe extracts, each ampule of which contained equal parts of these extracts, we elected to use one-half cubic centimeter of the extract of thymus.²

On admission, the interval between pains ranged from three to thirty minutes, with several recorded as "irregular." The appearance of the first pain after the injection was recorded in this series all the way from one to thirty minutes, later. The average time in the primiparas was nine minutes and in the multiparas nine and eight-tenths minutes. In the series of patients who had received thymo-

physin, the average time for the first pains to appear was five and five and nine-tenths minutes, respectively.*

Uterine contractions recurred from six and three-tenths to eight and six-tenths minutes. This showed quite a difference from the pituitary combination patients, in whom the pains recurred from one and six-tenths to three and six-tenths minutes, the shorter interval undoubtedly being due to the presence of the posterior pituitary extract.

The duration of these pains was seldom prolonged. In rare instances the pains lasted longer than those prior to the injection of thymus. With thymophysin, however, the pains were definitely prolonged, in some cases being noted as "continuous."

However, if neither the frequency nor the duration was unusually influenced, this could not be said of the intensity. There was a distinctly recognizable increase in the severity of the pains. Uterine contractions, which hitherto had been imperceptible to the patient, were now quickly recognized, and the patient would say that she felt the pain a little stronger. In some they were quite strong. However, after a lapse of a variable time, four to seven hours, unless labor had actually been strongly activated, the intensity gradually diminished. Usually labor progressed rapidly and was soon terminated. In the majority of those patients presenting no or irregular uterine contractions, a definite rhythmic interval was established, thereby facilitating progress.

The effect of thymus on the intensity of the pains was well marked. Prior to the administration of the extract, 26 were recorded as having weak, mild, or slight pains, 15 were having pains of moderate intensity, and 4 were having strong uterine contractions. Following the injection, only 4 had weak, slight, or mild pains, while 25 were having moderately intense pains, and 19 strong uterine contractions.

Full dilatation was effected, generally quite satisfactorily and rapidly. In the primiparas full dilatation was attained in eight and one-tenth hours and delivery in nine and eight-tenths hours, average. The multiparas responded in like manner, the average mean dilatation time being six and fifteen-hundredths hours, and the delivery time seven hours. In the thymophysin series complete dilatation occurred in the primiparas in five and twelve-hundredths hours, and in the multiparas in three and twenty-four-hundredths hours. This likewise demonstrated the effect of the addition of posterior pituitary lobe extract. The shortest lapse of time between the injection of thymus and the delivery was one hour and one minute; the longest, twenty-two hours and seventeen minutes. The former was a para ii, 2 fingers dilated, in whom the pains were irregular and weak. Following the injection

*For lack of space, it was found necessary to omit the detailed tables of cases submitted by the author.

of thymus, the contractions appeared every two minutes, lasting sixty seconds and were quite strong. The other patient was a para v, 1½ fingers dilated, in whom the pains came on every five minutes, but weak. After the injection, although the interval was still five minutes, the intensity slightly stronger and the contractions lasted thirty seconds, the effects of the thymus soon wore off, and in a short while, the pains appeared every ten minutes and a little while later the patient was noted as "resting quietly."

The blood pressure in these patients was unaffected, when recorded just prior to and within ten minutes after the administration of the extract of thymus. This is in accord with the method pursued in the thymophysin series. Unlike the findings in the latter investigation, which disclosed an average mean rise in the systolic pressure of 16 mm. Hg, and a diastolic of 9 mm. Hg, the pressure remained unchanged. In one case of toxemia, the patient had a pressure of 205/125. Following the injection of thymus, which was given with the thought of activating spontaneous labor, the pressure was 210/125. Under control of morphine sulphate she was finally bagged and delivered.

For the induction of labor, 6 patients, not in true labor, were given 0.5 c.c. of thymus extract. Apparently true labor was activated, but something was lacking to keep them going. After several hours, uterine contractions ceased. Each patient returned in a few days in true labor, the progress of which seemed to be quite rapid.

SUMMARY

Fifty patients received 0.5 c.c. of thymus extract, this being the only maximum dose with which we had any experience. Only 1 patient was 3 fingers dilated. The others ranged from no dilatation to 2½ fingers. Nine occipitoposteriors, 1 face, and 1 set of twins were encountered.

The frequency of the pains was only slightly increased. The duration of the pains was seldom affected. A definite rhythm was established. The intensity was distinctly increased. The patients stated that they experienced somewhat stronger pains after the administration of thymus. All of which resulted in earlier, full dilatation and delivery, not, however, as rapidly nor as forcefully as with thymophysin. The blood pressures were not affected.

CONCLUSIONS

It seems that thymus extract:

1. Has a definite action on the pregnant uterus.
2. Can be used to initiate perceptible, uterine contractions and maintain them for several hours.

3. If repeated at more frequent intervals or perhaps in larger doses, may not only bring on a "natural" labor but carry it to termination.

If this latter is true, it gives rise to the supposition that the developing fetal thymus, in utero, may have something to do with labor.

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901 WASHINGTON AVENUE.

REPORT OF A CASE OF BILATERAL OVARIAN TUMORS OF THE BRENNER TYPE*

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THE purpose of this paper is to add to the published cases of Brenner's tumor of the ovary a bilateral case, apparently the first to be recorded. Photographs and photomicrographs of each tumor are presented.

M. G., a colored widow, about seventy years of age, was admitted to the Memphis General Hospital on April 9, 1932, with the chief complaint of tumor of the abdomen.

Four months before admission she commenced to have frequent urination and constipation and noticed that her abdomen was enlarging. She had had cardiac palpitation on exertion and pain in the lower left abdominal quadrant at times.

Her teeth and tonsils were removed some years ago because she had articular rheumatism. Menses began at fourteen years of age, recurring every twenty-eight days, lasting three days, until the menopause was established fifteen years ago. Since then she has had no vaginal discharge, bloody or otherwise.

Patient had a marked arcus senilis. Her heart was slightly enlarged but there was no murmur. The apex beat was a little to the left and below the normal position. The lungs were normal. The abdomen presented a smooth symmetrical enlargement from the ensiform to the pubes, with filling of both flanks. Dullness on percussion was present everywhere except for an arc of resonance below the costal margin. A fluctuation wave was easily elicited. Temperature was 99° F., pulse 90, blood pressure 130 systolic, and 80 diastolic.

The external genitals, cervix, and uterus were in a state of senile atrophy. The abdominal tumor could be felt extending well down into the pelvis. To the right of the uterus could be felt a flattened hard mass about 6 cm. in diameter. It was separate from the uterus and apparently not connected with the other tumor.

The urine was normal. Red blood cells numbered 4,800,000. The hemoglobin was 82 per cent. The white blood cells numbered 8,100, of which 71 per cent were neutrophilic polymorphonuclears. The sedimentation time was two hours. Wassermann test was negative.

*Read before the Memphis and Shelby County Medical Society, February 7, 1933. Sections from this case were sent to Dr. Howard C. Taylor, Jr., of New York, who recognized them as of the Brenner type of ovarian tumor and sent them to Professor Robert Meyer of Berlin who confirmed the diagnosis.

Operation.—The patient was operated upon April 15, 1932. From the left side was removed a pedunculated pseudomucinous cystadenoma which filled the abdomen. Its capsule was smooth and of the typical pearly hue. There were no adhesions to parietal peritoneum or viscera. The right ovary was the seat of a solid tumor which macroscopically was thought to be a diffuse fibroma. There was no free fluid in the abdominal cavity.

Pathologic Examination.—*Macroscopic:* The right ovary was converted into a very firm, irregular, bluish white, translucent mass with smooth and glistening sur-



Fig. 1.—Photograph showing pseudomucinous cystoma type of Brenner's tumor of left ovary everted. Many cysts are seen, some of which are open.

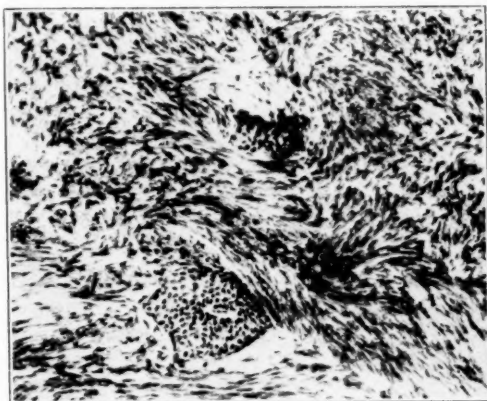


Fig. 2.—Section of tumor shown in Fig. 1. Note the ovarian type of stroma rich in cells and fibrous tissue with two nests of epithelial cells, characteristic of Brenner's tumor. Photomicrograph $\times 200$.

face resembling in a general way the ovary in shape. It measured 9 by 6 by 3 cm. and weighed 100 gm. A normal uterine tube was partly attached to the surface of the mass near the mesovarium.

On sectioning the mass, the knife met with considerable resistance. The cut surface consisted of fine, bluish white fibers enclosing small areas of pink tissue. The surface was everywhere translucent and very firm with several small, gritty areas (Fig. 1).

The left ovary was converted into a round, fluctuating mass with an intact outer membrane, whose surface was smooth and glistening. The mass measured 20 cm. in diameter and weighed 3,000 gm. A normal uterine tube was attached to its surface.

On sectioning the mass, it was found to consist of one large cavity with many smaller cysts projecting from the inner surface of its thick, bluish white, translucent fibrous wall. The large and smaller cysts were filled with a mucoid material and lined by a pink membrane, mostly smooth but in a few places mosslike (Fig. 1).



Fig. 3.—Lower epithelial nest of Brenner's type shown in Fig. 2, under higher magnification. Note in the periphery the single row of flat cells with dark, elongated nuclei and in the center coalescing, vascular spaces of degeneration partly surrounded by a single layer of flat cells with dark, elongated nuclei. Photomicrograph $\times 750$.



Fig. 4.—Section of tumor shown in Fig. 1. Note wall of cyst, with lumen containing pseudomucin and lined by pseudomucin-secreting, columnar epithelium. In the stroma are seen epithelial nests and strands of Brenner's type similar to those in Fig. 2. Photomicrograph $\times 200$.

Microscopic.—The right ovarian mass consisted mostly of stroma, resembling that of the ovary, rich in cells and fibrous tissue, running in various directions. Scattered through the stroma were small nests and strands sometimes joined by slender processes, of large, polygonal cells with pale cytoplasm and small, dark, round or elliptical nuclei. A single row of flat cells with dark, elongated nuclei, surrounded and separated them from the stroma. No intercellular stroma was demonstrated.

These cells sometimes showed small droplet spaces in their cytoplasm. Some of these cell nests showed in their center and at their periphery just visible and larger vacuolar spaces containing cellular and nuclear fragments. These spaces were partly surrounded by a single layer of flat cells with dark, elongated nuclei. Actual cysts were not seen. Blood vessels were scarce. A few small, partly calcified, necrotic areas were present. All tissues appeared benign. There was no sharp distinction between tumor and ovarian stroma (Figs. 2 and 3).

The cavities of the cystic mass of the left ovary contained pseudomucin and were lined by pseudomucin secreting columnar epithelium. This in places was of several layers, in others presented a papillary structure. A few mitotic figures could be seen, but there was no epithelial infiltration of the stroma. Here and there in the stroma were small nests and strands of large, polygonal cells similar to these seen in the right ovarian mass. The tumor was considered benign (Fig. 4).

Diagnosis.—Solid type of Brenner's tumor of right ovary. Pseudomucinous cystoma type of Brenner's tumor of left ovary.

Progress.—Patient's convalescence was uneventful, and she was discharged improved to the Out-Patient Department on April 29, 1932.

DISCUSSION

The right ovarian tumor of our case would be placed under Meyer's Group A, "Solid tumors of Brenner's type with or without cysts."

The left ovarian tumor of our case would be placed under Meyer's Group B, "Cystomas with nodules of Brenner's tumor in margins, with and without pseudomucin epithelium."

Ours is not only a bilateral case of Brenner's tumor of the ovary but it presents in the same case a solid type which stands at the one end and a pseudomucinous cystoma which stands at the other end of Meyer's series of Brenner's tumor.*

We are indebted for the photographs of these specimens to Mr. Joseph L. Scianni, University of Tennessee, Pathological Institute.

915 MADISON AVENUE

A CASE OF DOUBLE VAGINA, CERVIX, AND UTERUS†

LEONARD H. BISKIND, M.D., CLEVELAND, O.

(From the Gynecological Service, Mt. Sinai Hospital)

THIS unusual case was observed by the author through the courtesy of Dr. E. J. Braun of the Health Department of the City of Cleveland, and is presented here with his kind permission.

This patient, H. M. B., is an eighteen-year-old Cleveland-born girl, first seen as an institutional inmate May, 1932. The anomaly to be described was discovered on making a routine vaginal examination at the time of her admission to this institution.

Menses began at twelve years. After the first two periods these occurred regularly at approximately twenty-eight-day intervals and lasted three and one-half to four days. The flow was moderate in amount and no dysmenorrhea was present

*Meyer, R.: Arch. f. Gynäk. 148: 541, 1932.

†Presented before the Clinical Pathological Section, Cleveland Academy of Medicine, January 6, 1933.

except during rainy weather. In November, 1931, or about five years after the onset of her menses, there was a shortening of the intermenstrual phase to two weeks and a lengthening of the flow to five days; clots were noted for the first time. The patient attributed the change in menstrual routine to the fact that she was employed as a maid and had to do heavy housework. The semimonthly menses continued from November, 1931, to February, 1932. On February 5, 1932, a menstrual period began which lasted twenty-one days, followed by a two-day intermission and a subsequent flow for an additional five days. There had been no missed periods at any time prior to this and the patient vehemently denied any possibility of pregnancy. In the following four months she had only an eight-day rest between

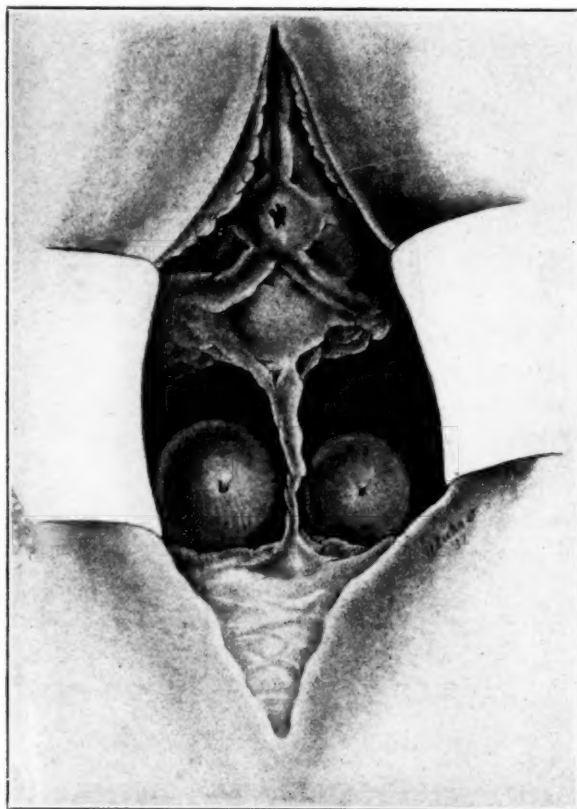


Fig. 1.

periods; bleeding occurred four days out of every twelve. Subsequently, in August, she had one period lasting twenty-two days; in September, two periods lasting five days each; in October, one period of fifteen days; in November, one period of eight days; in December, two periods lasting five days each.

The girl's height was 5 feet 8 inches; weight 164 pounds. Blood pressure, systolic 120, diastolic 70; pulse 84.

The mons veneris appeared to be fully developed, with no abnormalities in size or conformation and with the normal growth of hair. The right labium minus was 4.5 cm. in length while the left was only 2 cm. in length, the measurements being taken through the central portion. The clitoris showed no unusual formation and conformed in size to the other portions of the vulva. In the vestibule the tissue

about the urethral orifice occurred in thick folds, particularly posteriorly. The urethral orifice was prominent; the urethral papilla was more protuberant than normal, the meatus being stellate in shape. No vestiges of the hymen could be found. The Bartholin duct openings were visible and normally situated.

In the median line extending from the vaginal orifice superiorly and bisecting the vagina into two approximately equal parts was a septum, concave slightly at its free border. With the vaginal parts approximated, this septum folded upon itself vertically so that the anterior vaginal wall fell into its natural position with respect to the sides and floor of the vagina. The septum varied in thickness from 0.2 cm. to 0.6 cm. being about three times thicker anteriorly where it joined the upper portion of the vestibule than it was posteriorly, at the vaginal floor. The depth of both portions of the vagina was equal; the right side appeared to be wider in its central portion than the left by approximately one centimeter; the rugae were not unduly prominent and the color of the mucosa on both sides was a whitish red. The surfaces were coated with a normal amount of moisture.

The septum in the vagina extended superiorly to bisect the cervical portion of the uterus into two unequal parts. Each part consisted of a fully developed cervix, the right being somewhat larger than the left. Both cervices were those of nulliparas. Both canals were patent admitting probes of the usual size. Examination during a menstrual period showed bleeding from both cervices, with the flow from the right being greater than that from the left.

The fundus was retroverted and in midposition. It was somewhat larger than normal and irregular in shape, due to the fact that it was divided into two parts, the right being larger than the left. The depth of the right side was 7 cm. while the left was but 5 cm. With a probe in each cervical canal, extending into the fundus, an attempt was made to touch the probes together to determine whether one or two cavities existed. At no place along the entire uterus could the probes be approximated. The mesial wall was found on probing on either side to have much the same resiliency as the vaginal septum. The fundus was slightly to the right of the median line, probably due to the irregularity in shape. Neither tubes nor ovaries could be palpated. No abnormal masses were detected. A complete physical examination, excluding x-ray studies, failed to produce evidence of other anomalies in the pelvis or elsewhere.

A case is here presented of an unusual pelvic anomaly consisting of a double uterus, cervix, and vagina in an eighteen-year-old girl, presenting a history of polymenorrhea, menorrhagia, and metrorrhagia of about a year's duration. From the standpoint of treatment two distinct courses of action should be instituted. The one should be directed toward the correction of the menorrhagia and the metrorrhagia; the other should be of a surgical nature leading to the removal of the vaginal septum. The optimum time for surgical intervention is, of course, before pregnancy takes place.

SUBACUTE BACTERIAL ENDOCARDITIS COMPLICATING PREGNANCY AND THE PUERPERIUM

W. Z. BRADFORD, M.D., CHARLOTTE, N. C.

IN A RECENT issue of THE AMERICAN JOURNAL OF OBSTETRICS AND GYNECOLOGY, Mengert reports two cases of subacute bacterial endocarditis as a complication of pregnancy and after reviewing the literature has found only four other definitely established cases. An additional case was recently seen by us in consultation with Dr. Robert Leinbach, autopsy confirming the diagnosis.

White multipara, aged twenty-four, admitted to Charlotte Sanatorium Oct. 15, 1932, twenty days following the birth of her second child, with a temperature, pulse and respiratory rate of 104°, 168, and 32. In the seventh month of gestation the patient had developed a pyelitis of pregnancy, and for a few weeks prior to delivery had daily chills with high elevation of temperature, presumably from a flare-up of the kidney condition.

Patient had been delivered spontaneously at home by her family physician following a normal labor. Since delivery she had been suffering with daily chills, fever, and sweats during which time her general condition had steadily declined. She was referred to the hospital for investigation and treatment of supposed pyelonephritis.

The patient was pale and weak in appearance and extremely dyspneic. Examination was essentially negative except for a tachycardia of 168, temperature of 104° and evidence of passive congestion at the right base. Tentative diagnosis: Puerperal septicemia. An immediate transfusion of 300 c.c. whole blood was given and a blood culture taken.

The urine contained a faint cloud of albumin and a few hyaline and granular casts. The white cells were 18,500; R.B.C. 3,200,000; hemoglobin 62 per cent. The nonprotein nitrogen was 27 mg. per 100 c.c.

Cultures on blood agar plates showed 80 colonies of streptococcus of alpha type (viridans) per cubic centimeter of original blood.

The patient's condition steadily declined in spite of supportive treatment and transfusions, as shown by a rapidly progressive anemia, extreme dyspnea and toxicity.

Blood cultures showed 135 colonies of *Streptococcus viridans* per cubic centimeter of original blood on the day of death which occurred nine days following hospital admission.

AUTOPSY SUMMARY (DR. L. C. TODD, PATHOLOGIST)

1. Primary fatal lesion: Subacute bacterial endocarditis. Mitral valve vegetations (*Streptococcus viridans*) and large infected thrombus of valvular orifice and left auricular wall.

2. Terminal lesions: Multiple embolic infarction of spleen, left kidney, and liver (central nervous system not examined); bilateral serofibrinous pleurisy, pleural effusion, pericardial effusion, ascites; marked passive congestion of the lungs with a microscopic lobular hemorrhagic consolidation; pelvis negative.

3. Sections of valvular vegetation revealed marked hyaline changes establishing the duration of the pathology as at least several months.

DISCUSSION

This patient's past medical history was negative except that she had been told years before of the presence of a heart murmur and warned that she had "heart

disease." Three of Osler's criteria of subacute bacterial endocarditis were satisfied before death; namely fever, the existence of an old valve lesion, and positive blood cultures while the fourth, namely embolic phenomena, while not observed clinically was most extensively found at autopsy.

The case could readily have been dismissed as one of puerperal septicemia had blood cultures not been taken, and even with cultures it first appeared that this might be a true case of *Streptococcus viridans* septicemia following delivery. However, the autopsy findings established the endocardial vegetations, from the hyaline changes therein, as definitely antedating delivery by several months.

On this ground it is felt that here is a definite case of subacute bacterial endocarditis complicating pregnancy, possibly aggravated by labor and delivery, with death occurring early in the puerperium.

426 PROFESSIONAL BUILDING

CHRONIC APPENDICITIS SIMULATING CHRONIC ADNEXITIS DUE TO THE APPENDICULOOVARIAN LIGAMENT

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ACCORDING to Stedman,¹ the appendiculoovarian or Clado's ligament is a mesenteric fold running from the broad ligament on the right side to the appendix. Graves² defines the structure as "a fold of peritoneum running between the base of the appendix and the hilum of the ovary that is usually only rudimentary or not demonstrable but often quite definite, in which, it has been claimed, run connecting lymph channels between the appendix and the adnexa."

The literature disclosed a variety of names under which various authors have described the appendiculoovarian ligament. Beginning with Treitz,³ it was called the genitoenteric fold. Since this time, the Germans have generally spoken of it by this name, or perhaps even more commonly as the *ligamentum suspensorium ovarii*. The French have either followed Rouget,⁴ and called it the superior round ligament, or have followed Clado⁵ and Durand,⁶ and called it the appendiculoovarian ligament. In this country it has been most commonly called the appendiculoovarian or lumboovarian ligament. Careful study proves conclusively that the structures mentioned under these various names are identical.

Because of the paucity of reports in the literature and the casual brief description of this structure in only a few of the standard textbooks, the following protocol is reported.

Mrs. A. M., aged thirty-two, had been married fourteen years. She had had one pregnancy to term thirteen years previously, and had had two procured abortions in 1930 and in 1931 respectively. She began to menstruate at the age of sixteen, and the menses had been regular for the first two years. After marriage, the menstrual periods had been irregular, occurring five to ten days later than the expected time and of seven days' duration. Her last catamenia took place on Oct. 16, 1932. Venereal infection was denied. The family history was irrelevant. She had had no operations.

The patient was seen by the author on Oct. 27, 1932, complaining of a dull pain in the lower right quadrant of the abdomen. The onset of pain was seven years previously and accompanied by a sense of dragging in the right iliac region. During

the last five years the patient consulted a number of physicians for the alleviation of her abdominal complaint. The diagnosis of chronic adnexitis was invariably made and in each instance surgical intervention was advised after various conservative therapies had been employed. The other troublesome symptoms that the patient complained of were asthenia, anorexia, pyrosis, and backache.

Physical Examination.—The patient was well-developed and fairly well-nourished. The pupils were equal and reacted normally to light and accommodation. The head and neck were normal, and the nose and throat clear. The heart was normal in size, position, rate, and rhythm. The lungs were clear. The blood pressure was 124/82. Abdominal examination revealed tenderness at McBurney's point and in the right ovarian region lower down on digital pressure. On pelvic examination the anterior and posterior vaginal walls were found to be slightly relaxed, the cervix slightly hypertrophied, the uterus mobile, anteverted and of normal size and consistency. A tender cystic mass, the size of a walnut, was palpated in the right vaginal fornix. Nothing was felt in the left vaginal fornix.

Laboratory Examination.—The blood Wassermann was negative with both the alcoholic and cholesterol antigens. The blood sugar was 0.12 per cent. The blood examination showed: red cells 4,480,000, hemoglobin (Dare) 90 per cent, leucocytes 6,500, polymorphonuclears 66 per cent, large lymphocytes 5 per cent, small lymphocytes 27 per cent, eosinophiles 2 per cent. Sedimentation rate was sixty minutes. Urinalysis showed a faint trace of albumin, sugar and casts negative, pus cells two per high power field, a few calcium oxalate crystals, and a few epithelial cells.

Clinical Diagnosis.—(1) Chronic appendicitis; (2) right cystic ovary. Operation was advised and the patient referred to the Columbus Hospital.

On Nov. 10, 1932, the abdomen was opened by a subumbilical paramedian incision under ether anesthesia. The right ovary presented many cysts which were punctured with the point of a knife. Both tubes were found congested, in the premenstrual stage, but normal in every other respect. The appendix was about 6 cm. in length, very irregular in shape, slightly injected, and markedly angulated near its base. On closer examination, there was found a fold of peritoneum attaching the mesoappendix to the infundibulopelvic ligament of the right-sided adnexa, appearing as a distinct tense band. Upon severing this band the angulation of the appendix disappeared. An appendectomy and a V-shaped excision of the appendiculo-ovarian ligament completed the operation.

The microscopic examination of the appendix confirmed the preoperative diagnosis of chronic appendicitis.

The patient made an uneventful recovery and left the hospital on Nov. 20, 1932, feeling fine and happy.

COMMENT

The clinical significance of the appendiculoovarian ligament has been pointed out by Charpy,⁷ Clado,⁵ Kustner,⁸ Fraenkel,⁹ Deaver,¹⁰ Graves,¹¹ Craig,¹² DaCosta,¹³ and Rubin.¹⁴ To Clado, the clinical significance of the appendiculoovarian ligament depended entirely on the ability of its lymphatics to convey infection from the uterine appendages to the appendix, and vice versa. This lymph connection between the appendix and the adnexa has been denied.

This case presented several interesting features. It demonstrated that the appendiculoovarian ligament of Clado is not an independent entity, but rather a fold of peritoneum which is prolonged upward and outward from the infundibulopelvic ligament to the mesoappendix. The tenderness elicited in the right ovarian region was probably chiefly responsible for the diagnosis of chronic adnexitis. However, if a more painstaking examination, employing deep digital palpation abdominally, had been performed, tenderness at McBurney's point as well as tenderness over the

right ovarian region might have been elicited. In this case the chronic appendicitis was associated with an appendiculoovarian ligament, and tenderness, therefore, would have been found high up in the iliac region and at the same time would have extended continuously downward to the true pelvis.

180 EAST 111TH STREET.

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OVARIAN CYST AND PREECLAMPTIC TOXEMIA COMPLICATING THE SAME PREGNANCY

WINTON T. STACY, M.D., ST. JOSEPH, MO.

THE literature upon ovarian cyst complicating pregnancy is comprehensive but this report is offered in the belief that it makes a distinct contribution to the subject.

The patient, gravida i, aged twenty-eight, thinking herself pregnant, first consulted me March 30, 1932. Her last regular menstrual period was Jan. 21, 1932; but ten days prior to and ten days following the date of this last normal period, she spotted two or three pads. Heretofore, her periods had always been regular and painless. No intermenstrual bleeding. Next to last period was Dec. 25, 1931. She had been married three years, and used contraceptives until Jan. 1, 1932.

Her family history and past history were essentially negative, except a year ago she was in an accident, and the examining physician evidently felt a mass in the abdomen at that time because he asked if she were pregnant. The patient offered the information that she always had a large abdomen.

The only other symptom of pregnancy (besides missed period) was tender nipples. No nausea or vomiting. No frequency of micturition. No changes in disposition.

The upper abdomen was flat. There was a marked protuberance extending from the symphysis pubis to 1 cm. above the umbilicus. This tumor was within the true pelvis and extended to a point 18 cm. above the symphysis, pulled to the right; about the size of a four months' pregnant uterus; not tender and freely movable. No fetal heart tones or placental bruit were heard. No fetal movements were elicited.

Bimanual examination revealed a soft, short cervix. External os was closed. There was no ballotement. Douglas' culdesae seemed filled with a soft fluctuating mass. I was unable to make out the uterus.

Kahn, negative. R.B.C. 3,850,000; W.B.C. 9,500. Hb. 80 per cent. Urine negative. April 5-7 Friedman's test for pregnancy was positive.

Diagnosis: Ovarian cyst and pregnancy. The patient was so informed.

On April 8 findings were as above given. April 18 the patient complained of breathlessness and the superior margin of the tumor was 22 cm. above the symphysis pubis. At this time patient accepted consultation. The consultant, Dr. J. I. Byrne, who later performed the ovariectomy, confirmed the diagnosis.

There are two methods of treatment suggested for this condition. One advocates ovariectomy before term but after the second month in all cases; the other, ovariectomy and delivery at term. The dangers and complications of either method are well known. Each case should be individualized and, after due consideration, the plan of treatment that best fits the individual case carried out.

This patient, with an ovarian cyst of such magnitude, would offer serious complications at term, if she did not abort before term, and the likelihood of a twisted pedicle is great. Again, if operated in early pregnancy, there is a probability of an abortion, but we thought this probability less if operated than if allowed to proceed in pregnancy. Contrary to the opinion of several noted authorities ovariectomy was performed April 21, three months after her last normal period.

The abdomen was opened through a right rectus incision and a large ovarian cyst was removed. The pregnant uterus, about 5 to 6 cm. in diameter, rested upon this cyst which was incarcerated in the true pelvis and extended into the false pelvis, making it very difficult to feel the uterus on bimanual examination. The left ovary contained the corpus luteum cyst. This was not disturbed. The appendix was not examined. The wound was closed by interrupted sutures.

The pathologic report was as follows: The cyst measured 18 by 16 by 10 cm. The wall was thin, semitransparent, parchment-like and the outer surface was smooth. The inner surface was also smooth and glistened showing no evidence of papillary growths. The cyst formed one large cavity without trabeculas or daughter cysts, filled with cloudy amber colored fluid. No evidence of ovarian tissue was found in any area. The surface blood vessels were tortuous and somewhat flattened.

The cyst wall showed a lamellated, fibrous layer of varying thickness containing a moderate number of blood vessels running parallel to the lining membrane. This lining membrane consisted of a single layer of cylindrical epithelium which had central, deeply staining nucleus and rather clear cytoplasm. No evidence of histologic ovarian structure was found. This tumor was evidently a simple, single cyst of the ovary.

The patient made an uneventful recovery and left the hospital on the eleventh postoperative day. Her highest temperature was 99.6° on the afternoon of the operation.

This patient returned to the office regularly for prenatal care and observation. On admission to the hospital her hemoglobin was 75 per cent, otherwise her blood picture was normal throughout pregnancy. Her gain in weight, blood pressure readings, and urine examination findings were normal up to September 12. On this date the blood pressure reading and urine examination findings were normal, but she had gained five and one-half pounds in the past two weeks. There was slight edema of the feet and ankles. A 1200 calorie diet consisting of milk, vegetables, and fruit was ordered. In the next two weeks she gained 4½ pounds, blood pressure was 124/90 (a rise of twenty points in the diastolic) and the urine showed 2-plus albumin. The edema had not increased. There were no other signs or symptoms (headache, vertigo, visual disturbances) of impending toxemia.

A specimen of urine sent in on September 28 gave same findings as on the twenty-sixth. Rest in bed and a milk diet was ordered. On October 3, she had gained 3¼ pounds, blood pressure 126/86 and albuminuria 2-plus. A specimen of urine sent to the office on October 6 contained 3-plus albumin. Home call made on

that date. Blood pressure was 160/90. That afternoon it was 170/100. The patient's relatives were told the seriousness of the condition and that hospitalization was necessary, but they asked to leave her at home over the night to see if she would improve. This was done and the next day, October 7, 1932, her blood pressure was 180/106, and the patient was sent to the hospital.

Castor oil, quinine, and oxytocin, minims 2, per hypo every half hour, for eight doses failed to start labor. The blood pressure ranged from 146/90 to 170/102. The oxytocin had no noticeable effect upon the blood pressure. Twelve hours after the last dose of oxytocin, pantopon gr. $\frac{1}{8}$ was given. The next morning an 8 cm. Voorhees bag was inserted, and labor started within forty-five minutes. A baby boy weighing 6 pounds $8\frac{1}{2}$ ounces was delivered by low forceps eight hours and thirty minutes after the bag induction.

On admission to the hospital the urine contained 4-plus albumin. Nonprotein nitrogen, 27 mg. Phenolsulphonephthalein test, first, 18 per cent; second, 10 per cent; third, 15 per cent; fourth, 22 per cent; total of 65 per cent. Over two twelve-hour periods before delivery, the fluid intake exceeded the output by 100 to 150 c.c. During her stay in the hospital the blood pressure readings returned to normal and the urine from 4-plus to 1-plus albuminuria. The patient was dismissed on the twelfth postpartum day, with a blood pressure of 110/60, urine 1-plus, non-protein nitrogen 26 mg., and phenolsulphonephthalein test as follows: first, 55 per cent; second, 15 per cent; third, 5 per cent; fourth, trace; total 75 per cent. On October 24, three days after leaving the hospital, the urine showed only a faint trace of albumin.

This report is offered because the case presents several interesting features:

1. The result of the Friedman modification of the Aschheim-Zondek test was accurate in the presence of a large ovarian cyst.
2. Ovariectomy was performed three months after the last regular menstrual period.
3. Preeclamptic toxemia developed during the last month of pregnancy, making it necessary to induce labor.
4. Medical induction of labor failed but brought out the fact that oxytocin in this particular case had no demonstrable effect upon the blood pressure.

KIRKPATRICK BUILDING

THE USE OF DIOTHANE IN THE CONTROL OF AFTERPAIN IN HEMORRHOIDECTOMY

ARTHUR E. HERTZLER, M.D., HALSTEAD, KAN.

SATISFACTORY as novocaine is as a local anesthetic the pain following operations done under this anesthetic comes as an unhappy disillusionment. This is particularly noteworthy in operations for hemorrhoids. Commonly in pelvic operations, to which is added the removal of piles, whether done under general or spinal anesthesia, the afterpain lingers as the most memorable part of the experience. Because of this operators have been constantly on the lookout for some agent which would secure relief from the afterpain. The newest candidate for this office, diothane, seems to give unusual promise.

Bandler has recently published a report on its use as a local agent and Rider has discussed its chemistry. Apparently no one has published its action on tissues.

Injected into the skin it causes no burning but only slight pain from expansion of tissue. The degree of this is dependent on the size of the needle and the skill

with which the injection is made. When the wheal is formed the anesthesia is almost immediate and lasts four days. There is no zone of hyperanesthesia nor when it is subsiding as one finds in the case in the use of quinine anesthesia. When used with adrenalin, there is some peripheral hyperemia and a sense of soreness.

When injected into a rabbit's ear, after three days, the skin in the area injected has a perceptible edematous feel. The slide shows an amorphous edema with some perivascular round cell infiltration. The formation of granular fibrin as observed after the use of quinine is absent. The duration of the anesthesia is parallel with the persistence of this edema. It disappears in a week without leaving a trace.

For the control of afterpain following hemorrhoidectomy it must be injected into the base of the hemorrhoid at the point where it is to be severed just as one would use novocaine for the same purpose. If the operation is done as a part of more extended operation for which a general anesthesia is employed, the technic is the same. Following the injection of the diothane any operation desired may be done. It is important that the injection be made directly into the skin and mucous membrane. Merely depositing solution into the pararectal tissue does not give results.

Our experience has been that the afterpain is completely controlled for four days after operation and is lessened for some days after this time.

Just what effect this agent may have on the healing of wounds by first intention remains to be determined. Likely, like quinine, this will depend on the skill used in its use. Whether or not it will replace quinine for injection into nerves in neuralgias, likewise, requires further study.

REFERENCES

- Bandler*: Am. J. Surg. 19: 250, 1933. *Rider*: J. Pharmacol. & Exper. Therap. 39: 329, 457, 1930.

Erratum

In the article by Dr. Samuel J. Scadron in the January, 1934, issue there is an error on page 131, paragraph 4, line 3. "None of the 11 deaths occurred" should read "Nine of the 11 deaths occurred prior to the introduction of laparotrachelotomy and transperitoneal cesarean."

Special Article

CHILDBIRTH IN THE DAYS OF QUEEN ELIZABETH*

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THE reign of Queen Elizabeth, covering the second half of the sixteenth century, 1558-1603, was one of great change, not only in the political structure of Europe but also in the sciences. The revival of anatomy under Vesalius was influencing all medicine and while in obstetrics it was not to bear full fruit for a time, the beginnings were already evident.

While Elizabeth was popularly known as "the Virgin Queen," and most probably rightly so, sexual problems and those of childbirth were certainly important to her during most of her life. Before her birth there were prognostications as to the sex of the expected child, a most important question for a royal heir. A boy would have pleased Henry immensely, and probably would have atoned for the indiscretions of Anne Boleyn. But the predictions were wrong, and there were many who could not conceal their satisfaction. Eustace Chapuys, the ambassador of Charles V, was one of these, and in a letter to Charles, says:

... "On Sunday last, on the eve of Lady Day, about three o'clock in the afternoon, the King's mistress was delivered of a girl, to the great disappointment and sorrow of the King, of the Lady herself, and of others of her party, and to the great shame and confusion of physicians, astrologers, wizards, and witches, all of whom affirmed that it would be a boy."

(Quoted from F. A. Mumby: *The Girlhood of Queen Elizabeth*.)

What were the methods that might have been used to predict the sex of the unborn child? One way is given by Thomas Raynalde in *The Byrth of Mankynde*:

... "But if ye be desirous to know whether the conception be man or woman . . . if it be a male: then shall the woman with child be well coloured, and light in going, her belly round: bigger toward the right side than the left: (for commonly the man child lyeth in the right side, the woman in the left side) and in time of her bearing she shall better digest and like her meat: her stomach nothing so queesy nor feeble."

Elizabeth never married and, while there are rumors of illegitimate children, this is exceedingly doubtful. We know of her various affairs and gossip has linked with hers the names of Somerset, Leicester, and Essex. Chamberlin in his most interesting study, *The Private Character of Queen Elizabeth* has refuted these stories and, in addition, has brought together the medical history of Elizabeth. He had the advice of Sir William Osler, Sir Clifford Allbutt, Sir Arthur Keith and others and the consensus of opinion was that she was not, as usually stated, strong but was often seriously ill. She was of a highly nervous temperament and troubled with

*Read before the San Francisco Bay Counties Obstetrical and Gynecological Society, October 14, 1932.

menstrual disorders. The question has often arisen whether she was sterile or not. There is no evidence either way, but there were means in vogue of determining. Thus Raynalde says:

... "If ye be desirous to know whether the man or the woman be hindrance in conception: let each of them take a wheat and barley corns, and of beans of each seven the which they shall suffer to be steeped in their several urine: the space of xxiii hours: then take ii pots, such as they set gyly-flowers in; fill them with good earth: and in the one let be set the wheat, barley and beans, steeped in a man's water, and in the other the wheat, barley and beans steeped in the woman's water: and every morning the space of eight or ten days, let each of them with their proper urine water the said seeds sown in the forenamed pots, and marked whose pot doth prove, and the seeds therein contained doth grow, in that party is not the lack of conception, and see that there come no other water or rain on the pots: but trust not much this experiment."

But let us turn from the Virgin Queen to the more fruitful field of childbirth in general. This was practiced entirely by midwives, and that the results were far from satisfactory is shown by remarks in books of the time. Andrew Borde, in his *Breviary of Healthe*, 1552, tells of the bad conditions and says that midwives should be examined by the bishop with the counsel of a doctor of physic and instructed in their offices, "for and this were used in England there should not halfe so many women miscarry, nor so many children perished in every place in England as there be."

The purpose of the most important Renaissance obstetric work, Roesslin's *Rosengarten*, translated into English as *The Byrth of Manlynde*, was to improve midwifery. Thus the first translator, R. Jonas, said the book was to be read by the prospective mother, and she in turn was to instruct the midwife and her own maids. Concerning midwives he says:

... "There be many of them ryght expert, diligent, wyse, circumspecte, and tender aboute suche busynesse: so be there agayne manye mo full undyscreate, unreasonable, chorleshe, . . . Through whose rudenesse and rasshnesse onely I doubte not, but that a greate number are caste awaye and destroyed (the more petye)."

Now to consider this work in some detail and to relate it to the general knowledge of the day. Eucharius Roesslin, the original author, probably never delivered a child himself, as this was the province of midwives, and it was considered immoral for a physician to deal with such problems. His work, first published in 1513, was based on Greek sources, but which had been neglected until his time. The *Rosengarten* was very popular, being translated into many vernacular languages. The first English translation appeared in 1540. The second edition, somewhat revised, was brought out by Thomas Raynalde in 1545. In this form the work went through some twelve editions within a century. In his prologue he tells who should read the book and one wonders if the anatomic knowledge displayed was understood by the average person. Besides the prospective mother, her husband should also know these facts. He says:

... "It shall be no displeasure to any honest and loving woman, that her husband should read such things: for many men there be of so gentle and loving nature towards their wives, that they would be more diligent and careful to read or seek out anything that should do their wives good, being in that case, than the women themselves," . . .

He answers the criticism that idle, curious people may get hold of the book for its pornographic interest. He says that any good thing may be abused, and severely warns against such degradation. There were other works of this nature, in particular, *Aristotle's Last Legacy*, or *Aristotle's Masterpiece*, which is not by Aristotle at all. This little book in the same form and language, appears in modern editions and can be picked up at bookshops dealing in such subjects.

We know that false modesty of this sort prevented the spread of the anatomic knowledge so essential for sound obstetric practice. John Banister in his *Historie of Man*, "sucked from the sappe of the most approved Anathomistes," 1578, based on Vesalius and Columbus, says:

... "But because I am from the beginning persuaded that by lifting up the veil of Nature's secrets, in woman's shapes, I shall commit more indecencie against the office of decorum, than yield needful instruction to the profit of the common sort, I do here . . . rest." and so omitted the subject entirely.

But fortunately other anatomists were not so delicate and the discoveries of Vesalius were at an early date available in English. Thomas Geminus, in 1545, the same year as Raynalde's translation, brought out a Latin compendium of Vesalius, which was translated, in part, into the English, by Nicholas Udall, in 1553. This included the plates and descriptions of the female organs. These were a great advance on any previous knowledge, and it is significant that the same plates and descriptions are inserted by Raynalde into his work. This anatomic section does not appear in the original Roesslin. Dr. Crummer has shown that these plates were engraved separately from those in Geminus. The descriptions have been condensed from those of Vesalius, and are not the same in detail, as those in Udall's translation. They certainly give a fairly adequate idea of the generative organs and must have helped greatly in understanding the physiology of labor. Raynalde describes the skin, the abdominal muscles, the peritoneum, the matrix, and the ovaries, with their circulation. The matrix or uterus is described as having but a single cavity, and as greatly contracted "in women being not with child: . . . the which thing to some may seem incredible: yet by anatomy ye may see it to be true."

Of course they had no idea of the mammalian ovum, but considered that some sort of a seminal fluid flowed from the ovaries to the uterus at the time of conception.

Menstruation is described as follows:

"In English they be named terms because they return eftsoones at certain seasons, times and terms: and some name them there flowers: what name soever ye give unto it ye shall wit, that the thing meant thereby is nothing else but the issuing of certain blood comprehended in the veins of the matrice, thereby little and little, collected and gathered between term and term and so again at wont and accustomed times by nature expelled and sent forth."

They considered menstrual disorders as due to one of the four humours of the body, in other words, an endocrine dysfunction! There was an old belief that the menstrual discharge was infectious, and among some peoples the menstruating woman is taboo. Raynalde denounces this view:

... "Yet much more are to be detested and abhorred the shameful lies and slanders that Pliny, Albertus Magnus . . . and divers other more have written, of the venemous and dangerous infective nature of the woman's flowers or terms. The which all be but dreams and plain dotage: to rehearse their fond words here were but loss of ink and paper: wherefore let them pass with their authors."

There is not much concerning the development of the embryo, but there is a lengthy description of the fetal membranes. He describes implantation:

... "The seed then when it hath been a certain little space in the womb, by the natural heat, or rather by the inset and ingenyt virtue of that place, is environed and enclosed round with three divers coats, cauls, or wrappers."

Evidently most of his knowledge was gained from studying the membranes of lower forms, probably the chick, as he describes three membranes, with a well-developed allantois.

Now that we have seen in brief something of their knowledge of anatomy, let us see how they conducted a labor. They recognized that the normal method of presentation was vertex, but it would seem that they considered occiput posterior the most common. The various types of presentation are set forth in the birth figures, which have a long traditional history, similar positions being found in early manuscripts, and Paré reproduces some of the figures in identical postures. They seem to have had no idea of the mechanism of the engagement of the head at the superior strait or of the factors involved in its descent in the birth canal.

In the prenatal period the woman was cautioned to be careful of her diet, especially in the month before labor. She was to avoid becoming constipated, not to exercise overmuch, and not to stay too long in hot baths. Particularly he says:

... "But if it so be, that any infirmity or disease, swelling or other apostumation chance about the mother or the privy part, or about the bladder, as the stone, the strangury, and such like: the which thing may cause such straightness and coaretation that unneth great and horrible pain, the party can be delivered or discharged: in these cases it behooveth such things to be looked unto and cured before the time of labor cometh, by the advice of some expert surgeon."

Generally, the obstetric stool was used in delivery. The midwife anointed the canal with oil or the white of an egg, and, when she thought labor was at hand, she gently broke the membrane with her finger nail or with scissors or a knife. The midwife was to tell the woman when to hold her breath. She was also to

... "instruct and comfort the party ... with sweet words, giving her good hope of a speedful deliverance, encouraging and enstomaching her to patience and tolerance, bidding her to hold in her breath in so much as she may: also stroking gently with her hands her belly above the navel, for that helpeth to depress the birth downward." ...

In some cases she is to dilate the opening with her hands, anointed with oil. The continuation of the delivery is then described. After the child is born, the cord is cut three fingerbreadths from the navel, tied, and wrapped in a piece of wool with styptic powder. He cites an old belief from Avicenna that the number of wrinkles in the cord between the end and the navel signify how many more children the woman will bear. If there are none she will henceforth be barren. He is sceptical about this, declaring "but these sayings be neither in the gospel of the day, nor of the night." After this the child is then swaddled and its eyes are to be carefully washed out with warm water. This is to be repeated often.

Meanwhile the midwife is concerned with the delivery of the placenta. It is essential that this be expelled. Otherwise if retained it

... "will soon putrify and rot: whereof will eftsoon ill noisome and pestiferous vapours ascending to the heart, the brains and the midriff: through the which means the woman shall be shortwinded, faint hearted, often

founding and lying without any manner of moving or stirring in the pulses: yea and many times is plainly suffocated, strangled, and dead of it."

Various remedies are given which promote the expulsion, notably some provoking sneezing. A caution is given not to pull too hard "lest that with the second birth ye remove the matrice also." Postpartum fever is described:

... "It is also to be understood that many times after deliverance, happeneth to women other the fever or ague, or swelling or inflation of the body, other tumbling in the belly, or else commotion or settling out of order of the mother or matrice. Cause of the which things is sometimes lack of due and sufficient purgation and cleansing of the flowers after the birth, or else contrarywise overmuch flowing of the same: which sore doeth weaken the woman. Also the great labor and stirring of the matrice in the birth."

Remedies are given for this, but fortunately bleeding was not recommended. His best advice is to call in an expert physician and the following passage shows an interesting relation between the doctor and his patient:

... "Now seeing then that it ensueth by so manifold occasions and causes, it shall be meet that women in this case be nothing ashamed or abashed to disclose their mind unto expert physicians, showing them everything in it, as they know whereupon it should come: so that the physician understanding the woman's mind, may the sooner by his learning and experience consider the true cause of it and the very remedy to amend it."

Unnatural births—abnormal presentations, twins, a dead fetus or monsters—were the most feared and here the midwives had to be diligent. The various abnormalities are treated separately and usually the endeavor is to perform version, converting to a head presentation. Thus when one foot presents,

... "and in this case it behooveth the laboring woman to lay her upright upon her back, holding up her thighs and belly, so that her head be the lower part of her body: then let the midwife with her hand return in again the foot that cometh out first in as tender manner as may be, and warn the woman that laboreth to stirr and move herself, so that by the moving and stirring the birth may be turned the head downward, and so to make a natural birth of it, and then to set the woman in the stool again." ...

When version is impossible the midwife makes the best of it, delivering the child's feet first, but taking care to keep its hands at its side. There is no mention of podalic version, either in difficult labor or with placenta previa. Ambrose Paré at about this time had developed this method rather successfully.

With twins the concern is to get one out at a time, taking the one that is nearest to birth. When a dead fetus is diagnosed, it is to be expelled either by remedies, fumigation of the vaginal region, using the hoof or dung of an ass, or by surgical intervention. This was done by the midwife. Instruments that were used for this are shown in Paré's *Surgery*.

If, in spite of all the efforts of the midwife, the woman dies in labor and the child is still alive,

... "then turn her on the left side, and thereto cut her open, and so to take out the child. They that be born after this fashion are called cesares, for because they be cut out of their mother's belly. Whereupon also the noble Roman, Cesar the First, took his name" ...

The derivation of the word "Cesarean" is interesting. The New English Dictionary says it is from Julius Caesar who was born this way, but some derive it from the verb *caedo*, to cut. Certainly it was practiced before the time of Caesar, but it may have come from the *lex Caesare*, directing that all women dying in term should have the fetus removed whether it was alive or not.

There is a section on diseases of children, but since this is really not our concern, I will recite only the treatment of google eyes or looking askint. He directs that the child's cradle be so placed that the light falls on the child's face opposite to the deviation. "By this means the goggling of the eyes may be returned to the right place." A candle is to be placed in the same place at night. He also advises that bright yellow and green cloths be placed on the contrary side

... "for the child shall have pleasure to behold these strange colors and returning the eye sight toward such things, it shall be occasion to rectify the sight again."

The work ends with a section not usually found in modern works on the subject, but which might be pertinent if read by the lay public. This consists of beauty remedies, for removing freckles, unsightly hair, warts, and to correct bad breath and "the rank savour of the armholes." This phase of obstetrics has now become the province of advertising experts.

From this work, which was the only important one on the subject in English at this time and, if we can judge from the many editions, exceedingly popular, we gain some idea of the way in which childbirth was conducted, and something of its difficulties. They knew nothing of the dangers of infection and the maternal mortality must have been high. Fortunately, for them, deliveries were done in the home so they were spared "hospital fever," the scourge of women in labor, at a time when some of the greatest technical advances were being made. Infant mortality was also great and was a matter of concern to the Queen. The crowded and unsanitary conditions of the cities was a large factor. The knowledge of anatomy was to contribute greatly to a fuller understanding of the problem, and to the better management of labor. The invention of forceps in the next century was probably in part a result of this.

In general, I think we can say that, while the restriction of this art to midwives alone is to be censured, a work such as this was of inestimable value to them and at least made the practice more scientific. The concern of physicians in such affairs was bound to bring them to feel that childbirth was a medical and surgical problem and, false modesty aside, it was their duty to concern themselves in this practice. We know that this was soon to be the case, to the great advancement of the science. This little work played its part and the generally conservative attitude was in the line of the best medical thought.

Department of Maternal Welfare

CONDUCTED BY FRED L. ADAIR, M.D., CHICAGO, ILL.

MATERNAL MORTALITY STUDY FOR CLEVELAND, OHIO*

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A COMPLETE and detailed study has been attempted of every puerperal death occurring within the confines of the city of Cleveland during 1931. This includes the deaths of women from all causes dependent more or less directly upon pregnancy at any stage of gestation and upon parturition. It requires a careful scrutiny of every death recorded as puerperal by the local Bureau of Vital Statistics of the City Division of Health. It includes so-called "criminal abortions," which are usually classified as homicides. These are as truly puerperal as those following self-induced or therapeutic abortions, and they should be included in any complete study of puerperal mortality. Every coroner's case involving the puerperal state has been investigated thoroughly. The deaths of all females between the ages of fifteen and fifty years also have been checked against the live and stillbirths. Every association between them, suggested by similarity of name, place of residence or of birth, and time of birth, has been followed up to determine possible puerperal relationships. The official number of puerperal deaths in Cleveland during 1931 was 117. This study revealed 151 puerperal deaths, including the 12 criminal abortions, which could be so classified.

Basic data in addition have been secured from individual physicians, midwives, hospital records, and the Visiting Nurse Association. The items have been recorded on schedules prepared by an advisory committee of the United States Children's Bureau. They have been analyzed in the office of the Cleveland Child Health Association. This study was undertaken with the approval of the Academy of Medicine of Cleveland and was made possible by the thorough cooperation of the Cleveland Division of Health, individual physicians, maternity and general hospitals, coroner's office, and the Visiting Nurse Association.

During 1931 there were 16,279 live births and 592 stillbirths.† Of these born alive, 496 died under two weeks of age and 527 under one month. There were 151 puerperal deaths giving a puerperal mortality rate of 9.3 per thousand live births or 8.9 per thousand live plus stillbirths. The official puerperal mortality rate based upon 117 recorded deaths was 7.2 per thousand live births.

It is highly desirable that a distinction be made between viable births, which may be expected to survive, and those which have little possibility of living. In

*Complete paper with tables and charts presented before the Obstetrical and Gynecological Section of the Academy of Medicine of Cleveland, March 29, 1933.

For lack of space it is not possible to include the basic tables, but copies of these may be obtained from the Cleveland Child Health Association, 1900 Euclid Avenue, Cleveland, at ten cents per copy.

†Official figures. Six cases listed officially as stillbirths were found on further investigation to be live births.

this study there were puerperal deaths following 50 abortions, 8 ruptured ectopics, and 7 undelivered, all under twenty-eight weeks of uterogestation, and 2 undelivered over twenty-eight weeks of uterogestation. This leaves only 84 viable births. A maternal mortality rate based on this number would be 5.2 per thousand live births. Thus it is seen that after removing all abortion deaths there remains a fairly high maternal mortality rate.

Of the 8 ruptured ectopics, 5 patients died from hemorrhage, 2 from hemorrhage and peritonitis and one from peritonitis alone. Laparotomy was performed on 6 of the patients and 2 died without operation. In the 9 undelivered cases there was one death each from the following causes: anesthetic shock, acute dilatation of heart, angina pectoris, bronchopneumonia, diabetes mellitus, eclampsia, pulmonary embolus, sepsis following tuboovarian abscess, and sepsis following operation for fibroid uterus, shown to be a pregnancy.

The cause of death among the 151 puerperal deaths was confirmed by autopsy in 31 cases and by partial autopsy or operation in 32 cases.

In this study every fetus under twenty-eight weeks of gestation is considered as nonviable and its premature expulsion is classified as an abortion. Of the 50 puerperal deaths following abortion 16 were spontaneous, 14 self-induced, 12 criminal, 6 therapeutic, and 2 of unknown origin. The primary causes of death following these abortions were sepsis alone in 35 cases, hemorrhage alone in 7, sepsis with hemorrhage in 2, and one case each of embolism, lung abscess, myocarditis, toxemia, intestinal obstruction, and pulmonary tuberculosis. It is recognized fully that deaths reported under any of these captions may have sepsis as a primary condition. This is the case especially in embolism, lung abscess, and intestinal obstruction.

Abortions make up one-third of the total puerperal deaths. In over 70 per cent of these abortions sepsis was the primary cause of death. In 42 of the abortion cases there was no prenatal care, in 5 the care was inadequate, and in only 3 cases could it be considered adequate. Following 31 of the abortions some operative procedures were instituted. In very few of the abortions was it possible to secure any prenatal care. It is misleading, therefore, to make any comparison of maternal mortality in the community at large, where all deaths from abortions are included, with the mortality among maternity cases under intensive care after the middle of pregnancy. Abortion undoubtedly has been on the increase since the World War. This condition may be one of the main factors in the stationary or increasing puerperal mortality rates in this country.

It can be shown from other data* that it is fallacious to compare maternal mortality rates in the United States with those in other countries, where definition of terms, methods of classification, and interpretation of records differ widely. Even in the Cleveland study 33 puerperal deaths of the 151 were subject to diagnoses or interpretations different from those recorded in the original death certificates.

In this series of 151 puerperal deaths 135 of the women were married, 12 single, 2 divorced, and 2 widowed. There were 131 white women, 19 colored, and one of doubtful color. While 8.6 per cent of the total births occurred to negro women, 12.5 per cent of the deaths occurred among them. The chief occupation of 130 of the women was housework.

Of the 1,679 registered physicians in Cleveland, 865 attended one or more of 16,014 live and stillbirths during 1931, or 95 per cent of the total births. Forty-eight

*Data collected by the Division of Vital Statistics, U. S. Bureau of the Census and prepared in photostatic copy, August, 1931. *Assignment by the United States and Certain Foreign Countries of Cause of Death on Identical Copies of Selected Death Certificates, 1927, on which One or More of the Causes Stated Was Puerperal in Nature.*

per cent of the physicians attended five or less live births during 1931, 67 per cent attended ten or less, and 83 per cent attended twenty or less. In other words only about one-fifth of the physicians had over twenty live births.

Eighty-three physicians listed as obstetricians and gynecologists attended or supervised approximately 46 per cent of the live births, 758 general practitioners and others* 49 per cent, and midwives 5 per cent. Nine osteopaths handled 27 live births in 1931.

Of the 267 physicians handling 574 of the stillbirths, 18 per cent were obstetricians and gynecologists, 63 per cent general practitioners, and 9 per cent others. The obstetricians and gynecologists had 44 per cent of the stillbirths, general practitioners 42 per cent, and others 12 per cent, midwives 1.5 per cent, and no medical care 0.5 per cent.

The 151 puerperal deaths occurred in the practice of 109 physicians and 9 midwives. Fifty-five of these deaths occurred in the practice of 33 physicians listed as obstetricians and gynecologists, 87 deaths in the practice of 76 general practitioners and others, and 9 deaths in the hands of 9 midwives. In other words, 36 per cent of the maternal deaths were handled by specialists, 58 per cent by general practitioners and others, and 6 per cent by midwives.

Approximately 60 per cent of the total live and stillbirths (10,115 confinements) occurred in 31 hospitals. Eighty-five per cent of the puerperal deaths occurred in these same hospitals. A careful scrutiny of every puerperal death revealed that, of the women who died in the hospitals, 76 per cent were referred from the home to the hospital because of known pathologic conditions. A considerable number of the cases had been in the hands of more than one physician before entrance to the hospital. Practically all of the infected abortion patients died in hospitals.

The maternal mortality rates varied greatly depending upon the nature of the hospital, composition of staff, and selection of cases. The exclusively maternity hospitals showed the lowest rates (combined rate 5.9 per thousand live births) as contrasted with the general hospitals with maternity licenses (rate 14.4). Six non-maternity hospitals had 9 living births and 2 stillbirths with 17 puerperal deaths, due to the fact that these hospitals take only emergency maternity cases and cases before viability. If comparison be made between the hospitals on the basis of viable births only, the rates in the maternity and general hospitals with maternity wards closely approach one another. In the strictly maternity hospitals and in some of the general hospitals it is the rule not to take the abortions or septic cases, but to refer them to the city hospital. As a result the city hospital, to which all types of cases are referred, had an exceptionally high puerperal mortality.

The puerperal mortality rate for the 6,516 live home cases was 3.5 per thousand live births as compared with 13.1 in the hospitals as a whole. It should be noted, however, that practically all the deaths following abortion and many of the complicated deliveries occurred in the hospitals. However, if all abortion deaths are eliminated, the hospital rate still remains higher than that in the homes from causes mentioned in previous paragraphs.

There were 98 registered midwives in Cleveland in 1931. Of these 87 attended 818 live births and 9 stillbirths. Nine puerperal deaths occurred among cases with which the midwife had anything to do. Every puerperal death in which a midwife contact could be traced was credited to the midwife and not to the doctor signing the death certificate. Five of the 9 puerperal deaths followed criminal abortions induced by midwives and later turned over to physicians. All of these died of sepsis. One midwife's patient with a difficult impacted shoulder, was delivered by a physician and died of sepsis. Three deaths occurred suddenly, apparently from

*Others include surgery, internal medicine, pediatrics, urology, anesthesia, and other specialties in addition to those not classified.

emboli, on the third, eighth, and thirty-sixth day after normal deliveries. Suspicion of infection is thrown upon the late emboli. If we exclude the abortion deaths, we find that the puerperal mortality rate among viable cases in midwives' practice (5.0) is still lower than that among physicians' cases (6.3 per thousand live births).

The primary causes of death among the 84 women giving birth to viable fetuses were as follows: puerperal septicemia 19; various accidents of labor including cesarean section, instrumentation, surgical interference, version, etc. 18; toxemias of pregnancy 12; puerperal hemorrhage 8; emboli 8; other accidents of pregnancy 6; lobar pneumonia 4; pulmonary tuberculosis 2; puerperal psychoses 2; and one death each from scarlet fever, influenza, cerebrospinal meningitis, chronic nephritis, and anesthetic shock. One of the undelivered patients died of bronchopneumonia, and the other was an anesthetic death.

As contributing or secondary causes, accidents of labor took first place with 21 cases, pneumonia came second with 15, and diseases of the heart third with 14. It is seen, therefore, that while a number of the different conditions may play secondary or contributing parts, the puerperal state itself was mainly responsible for the deaths, with sepsis as the leading cause and accidents of labor and toxemias as close seconds.

There were twelve deaths following classical cesarean section and four following extraperitoneal section. Eight deaths followed internal podalic version and extraction, and seven followed breech extraction. The number of deaths following forceps delivery were as follows: "Prophylactic forceps" 4, low forceps 16, midforceps 3, and high forceps 1, a total of 24 forceps deliveries. In only 28 cases were the deliveries spontaneous.

The greatest number of puerperal deaths occurred in patients between twenty-five and thirty years of age (47 cases) and the next to the greatest number in those between thirty and thirty-five years; although almost as many occurred in patients between twenty and twenty-five years of age. One girl was sixteen years old and one woman was forty-five.

A study of the age distribution of puerperal deaths is very instructive. An analysis has been made of the deaths, separating the abortions from the viable births. They are expressed as rates per thousand total births in each five-year age group. The rate for abortion cases is highest in the fifteen- to twenty-year group and does not vary markedly in the other age groups. In the viable cases, however, the rate is lowest in the twenty- to twenty-five-year period and increases gradually with each advancing age group. The rate in the fifteen- to twenty-year group is somewhat greater (7.3) than the twenty- to twenty-five-year group (6.0).

The relation of puerperal mortality to the parity of all the cases has been analyzed also. The rate for the abortion cases remains about the same (2.4 to 2.7 per thousand total births) up to para v, where it is 4.8. This increases to 6.4 for para vii. In viable cases the rate for primiparas is 4.2. It is low for para ii and iii and becomes high (9.0) for para iv, remaining high for the greater parities.

The births, stillbirths, and puerperal deaths for 1931 have been analyzed by census tracts and have been distributed by residence of mother into fourteen groups depending upon equivalent monthly rentals. These were determined by Howard Whipple Green from data collected in the United States Census of 1930.* The lowest economic areas include those census tracts with equivalent monthly rentals of from \$10 to \$15, the next from \$15 to \$20, and the following areas increasing by steps of \$5 up to \$100.

In hospitals births to women in the \$10 to \$15 economic area make up 27.7 per cent of the total births in that group, in the \$35 to \$40 area 51.3 per cent, and in

*Population Characteristics by Census Tracts, Cleveland, Ohio, 1930, Cleveland Plain Dealer Publishing Company.

the \$75 and over area 99 to 100 per cent. In the home deliveries physicians attended 41.5 per cent of the births to women in the \$10 to \$15 economic areas, 52.8 per cent in the \$20 to \$25 areas, 51.9 per cent in the \$25 to \$29 areas, 47.7 per cent in the \$35 to \$40 areas, and 0.3 per cent in the \$75 to \$100 areas. Midwives attended 30.8 per cent of the births in the \$10 to \$15 economic areas, 6.8 per cent in the \$25 to \$30 areas, 1.1 per cent in the \$45 to \$50 areas, and only 0.2 per cent in the \$75 to \$100 areas.

CONCLUSIONS

1. Factors entering into puerperal mortality are so interwoven with the social, economic, and cultural fabric of the community that it is impossible to evaluate them without a detailed study of each individual case.

2. Comparison of maternal mortality rates for different communities is misleading unless definition of terms, methods of collecting data, and interpretation of records are comparable.

3. Deaths following abortion should be separated from deaths after the twenty-eighth week of uterogestation to gain a true picture of the situation.

4. The midwife, aside from abortions, plays a relatively minor rôle in contributing to the high maternal mortality rate.

5. Sepsis, toxemias, and hemorrhage play the major tragic rôles, and these are associated largely with hurried, operative, and bizarre obstetrics.

6. Prenatal care and hospitalization are accessories to the actual obstetric situation. They may or may not be associated with a low maternal mortality, depending upon the type of medical, nursing, and hospital care afforded.

7. Not every maternal death is, at present, preventable. Fundamental changes must take place in the socioeconomic order and more complete medical knowledge and skill be available in order to approach this ideal.

1900 EUCLID AVENUE

Books Received

THE FIRST TWO YEARS. A study of 25 babies. By Mary M. Shirley, assistant professor of psychology, Randolph-Macon Woman's College. Vol. II. Intellectual Development. University of Minnesota Press, 1933.

METASTASEN UND REZIDIVE IM KNOCHEN BEIM GENITALCARCINOM DER FRAU. Von Dozent Dr. E. Philipp and Dr. G. Schaeffer, Universitäts-Frauenklinik Berlin. Mit 37 Abbildungen. Verlag von Julius Springer, Berlin, 1933.

MYSTERY, MAGIC AND MEDICINE. The Rise of Medicine from Superstition to Science. By Howard W. Haggard, M.D., Yale University. Doubleday, Doran & Co., Garden City, N. Y., 1933.

HANDBUCH DER GYNAEKOLOGIE. Dritte, neubearbeitete und erweiterte Auflage des Handbuches der Gynaekologie von J. Veit. Vierter Band, erste Hälfte. Bearbeitet von A. Laqueur, W. Rump und H. Wintz. Mit 272 Abbildungen. Die physikalische Therapie in der Gynaekologie. Verlag von J. F. Bergmann, München.

DIE LUFTEMBOLIE. Von Dozent Dr. Siegfried Hoffheinz, chirurg. Klinik Leipzig. Mit 50 teils farbigen Abbildungen. Verlag von Ferdinand Enke in Stuttgart, 1933.

Department of Reviews and Abstracts

CONDUCTED BY HUGO EHRENFEST, M.D., ASSOCIATE EDITOR

Selected Abstracts

Oxytocics

Bourne and Bell: *Uterine Inertia*, J. Obst. & Gynec. Brit. Emp. 40: 423, 1933.

There were 49 cases of genuine, primary inertia in a series of 4,500 labors. Forty-three of these were primiparous women, and 6 were parous. The pregnancies of 36 of them were completely normal, and in 34 of the women, the baby's occiput was anterior. Of the 49 women 13 labors were induced, and it was found that inertia followed induction more often than spontaneous onset of labor. Premature rupture of the membranes occurred in 30 cases, and a first stage longer than one hundred hours occurred in 17. Eight patients had manual dilatation of the cervix and 8 lost more than 600 c.c. of blood. Fear is mentioned as one of the causes of uterine inertia. The mechanism of this is probably through the liberation of adrenalin, which is known to have a relaxing effect on the pregnant uterus.

The author concludes that uterine inertia is probably one of the chief indirect causes of obstetric disasters. The treatment of the majority of cases of inertia is by the expectant use of sedative drugs. The chief danger lies in too early interference which results in lacerations, shock, hemorrhage, and sepsis.

WILLIAM F. MENGERT.

Legiehn, H.: *Potentiation by Combinations of Oxytocics*, Monatschr. f. Geburtsh. u. Gynäk. 91: 436, 1932.

Legiehn found that there was a potentiation of effects not only from the combination of pituitary extract and quinine but also from combinations of ergot preparations and quinine. The effect is dependent upon the state of irritability of the uterus. If quinine has very little effect there is only a simple addition of the effects of the combination of drugs. The potentiating effect is due to the fact that the more irritable the uterus the greater the stimulating effect of the drugs used. A fixed and customary combination of oxytocics should not be used because with increased irritability of the uterus, there is danger of a toxic effect, especially tetany of the uterus. From the pharmacologist's point of view the different oxytocics have definite indications. Quinine should be used to initiate uterine contractions and in the first stage of labor. Pituitary extract should be employed in the second stage of labor, and at this time it may be combined with quinine. Pituitary extract and ergot preparations should be employed in the third stage and for hemorrhages due to lack of tonicity of the uterus.

J. P. GREENHILL.

Fecht: The Question of Thymophysin, Zentralbl. f. Gynäk. 55: 1467, 1931.

One-half to one cubic centimeter of thymophysin was given intramuscularly to each of 32 parturient women as soon as labor pains were definitely established. In every case a decidedly deleterious effect upon the fetal heart tones was noticed a short time after injection. The fetal heart rate would rise so rapidly that counting was impossible and would suddenly sink below 100 beats a minute, giving a typical picture of intrauterine asphyxia. The amniotic fluid was meconium stained, thus substantiating the idea that the fetus was in danger. There were nine asphyxiated children in the 32 cases. Eight, including one which had primarily weak pains, developed a tetanic uterus which lasted from two to three minutes, a short time after injection. Labor was shortened in five cases. During the second stage, only one bad result was observed. The uterus went into a tetanic contraction, and a hasty narcosis and forceps operation were necessary. The author concludes, "I come to the conclusion that the use of thymophysin presents a frank and unnecessary danger. My own observations and the communications of my colleagues impel me to give this warning."

WILLIAM F. MENGERT.

Willi, C.: Our Experience With Thymophysin, Monatschr. f. Geburtsh. u. Gynäk. 93: 42, 1932.

Willi has employed thymophysin in about 200 obstetric cases and considers it to be an excellent means of overcoming primary uterine weak pains in the first stage of labor. However, not more than 0.3 to 0.5 c.c. should be given at one time, and this dose should not be repeated in less than one or two hours, if the pains have again decreased in strength and frequency. The drug should only be used for strict indications and under these circumstances it is without danger. Its action may be aided by the use of quinine. It is not satisfactory for the induction of labor in cases where the uterus is not sensitized. The author does not agree with Temesváry that the drug should be used almost routinely in normal labor cases after pains have begun.

J. P. GREENHILL.

Schaefer, W., and Gundlach, V.: Our Experience With the Oxytocic Thymophysin, Monatschr. f. Geburtsh. u. Gynäk. 95: 26, 1933.

In 102 cases the writers tested the efficacy of thymophysin. Of these patients 50 had primary and 52 secondary weak pains. The drug was used in both the first and second stages of labor and not more than 0.5 c.c. was used at one time. In the latter part of this investigation the dose was reduced to 0.3 c.c. These doses were repeated every half hour as indicated. Among 66 trials in the first stage the drug gave good results in 46; but in 20 cases the pains were not appreciably influenced. Among 36 trials in the second stage, the drug was helpful 25 times. During the first stage the fetal heart tones three times dropped below 100; but they quickly returned to normal. An equal number of fetal disturbances occurred in the second stage and again the heart tones increased in rate without the necessity of any interference. In 5 cases there were prolonged uterine contractions during the first stage and in one instance it lasted twelve minutes. In the second stage there were 3 instances of prolonged uterine contractions and in one of these forceps had to be applied to deliver the child. In all the cases of spasm chloroform was administered. Because of these disturbances the authors reduced the dose from 0.5 c.c. to 0.3 c.c.

The authors have never observed any harmful effects in the mothers not even in cases of eclampsia. They emphasize that they are opposed to the routine use of

this drug in cases which are progressing normally because harm may result to mother or child. In cases of uterine atony, however, thymophysin is very useful.

J. P. GREENHILL.

Traube, Karl: Clinical Experience With Combined and Fractional Oxytocic Posterior Pituitary Extracts (Thymophysin and Orasthin), *Monatschr. f. Geburtsh. u. Gynäk.* 93: 301, 1933.

In a series of 734 cases thymophysin was used by Traube. The drug was useful only after labor pains had begun. In 602 cases the drug was used in the first and in 132 cases in the second stage. In 408 cases a single intramuscular injection of 5 Voegtlin units sufficed to produce the desired result. In 88 cases (13 per cent) tetanic contractions of the uterus resulted and chloroform had to be administered to relax the severe uterine cramp. With the use of smaller doses, this complication decreased in frequency. In 24 cases there was severe asphyxia and one infant died, but in a previous series of 94 cases where increased doses had been used 3 infants had died. Because thymophysin is not without danger for the child the author warns that only small doses should be administered and that the fetal heart be controlled carefully. He prefers to sensitize the uterus with small doses of quinine rather than give repeated doses of thymophysin. Orasthin was no more efficacious in initiating labor than thymophysin. It was not as effective as thymophysin in the first stage of labor.

J. P. GREENHILL.

Hofbauer, J.: Thymophysin, *Zentralbl. f. Gyäk.* 57: 872, 1933.

The author reviews the various critical analyses of the use of thymophysin in America, and quotes a number of clinics to show that there do not seem to inhere the special virtues in a mixture of thymus and pituitary as are claimed by Temesváry. He asserts that thymophysin is nothing else but the equivalent of a weak solution of posterior pituitary extract. The addition of thymus to pituitary extract does not add any factor of safety to the pituitary extract. He concludes: "The alleged superiority of thymophysin over the usual pituitary extracts will not stand before an unprejudiced critique. The clinical results from the use of thymophysin depend entirely upon its content of hypophyseal extract."

WILLIAM F. MENGERT.

Item

American Board of Obstetrics and Gynecology

Written examination (Group B. candidates) various cities United States and Canada, April 7; Oral (all candidates) Cleveland, June 12, immediately prior to meeting of American Medical Association. Reduced railroad rates will be available and all applicants are urged to register in the Section and attend the scientific sessions.

For further information and application blanks for these examinations apply to the Secretary, Dr. Paul Titus, 1015 Highland Building, Pittsburgh (6), Pa.